A PROSPECTIVE STUDY OF PEPTIC PERFORATION IN BUNDELKHAND REGION IN REFERENCE TO PREVALENCE OF H. PYLORI IN PEPTIC PERFORATION

THESIS

FOR

MASTER OF SURGERY





DEPARTMENT OF SURGERY

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BUNDELKHAND UNIVERSITY

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2007

DR. VINEET KUMAR VERMA

Dedicated

to

Respected Teacher's

Parents, Friends

&

My Wife

DEPARTMENT OF SURGERY

M.L.B. Medical College, Jhansi

Certificate

This is to certify that work entitled ***"A PROSPECTIVE STUDY OF PEPTIC PERFORATION IN BUNDELKHAND REGION IN REFERENCE TO PREVALENCE OF H. PYLORI IN PEPTIC PERFORATION"*** which is being presented as Thesis for M.S. (Surgery) Examination 2007 of Bundelkhand University, Jhansi, by ***Dr. Vineet Kumar Verma*** in the Department of Surgery, M.L.B. Medical College, Jhansi.

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The observation recorded were periodically checked and verified by me.

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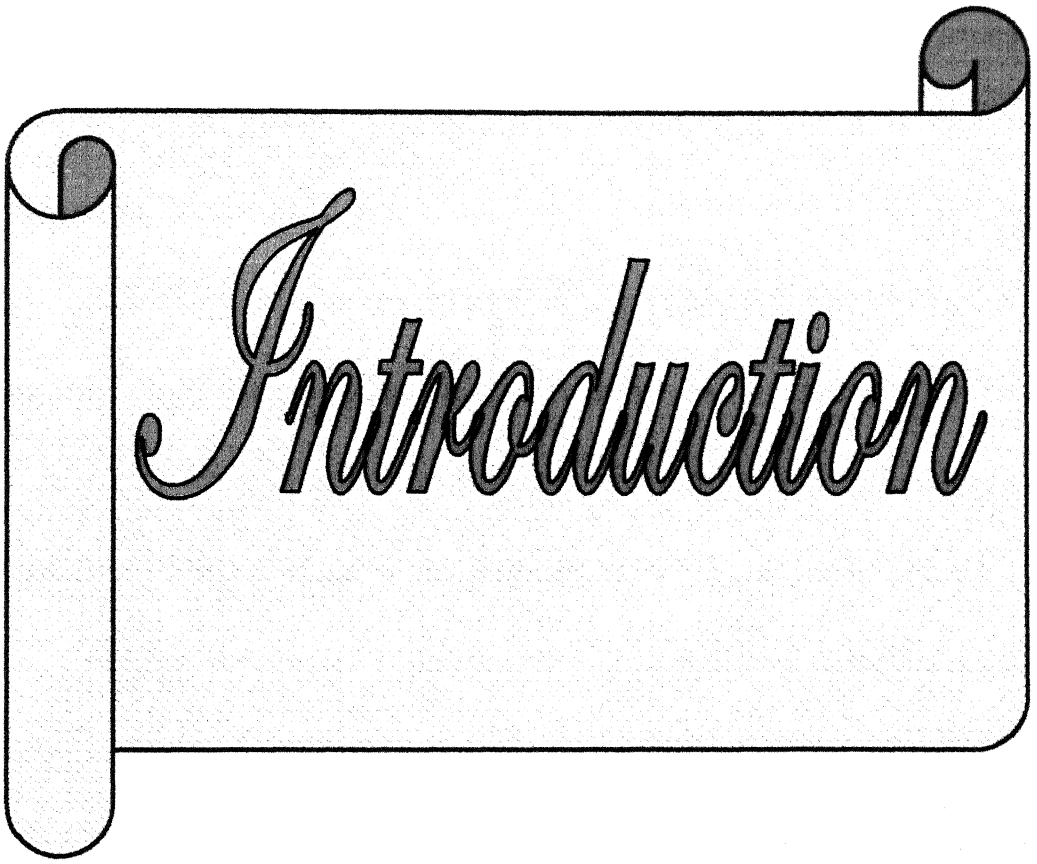
In the last but not the least I would like to thank all my patients who were the basis of my study.

Vineet Kumar Verma

Dated: **(Vineet Kumar Verma)**

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Introduction

INTRODUCTION

Peptic ulcers are most often solitary chronic lesions that occur at any level of GI tract exposed to aggressive action of acid peptic juices or a decrease in the mucosal resistance.

An ulcer is defined as a persistent discontinuity of an epithelial surface that can occur in skin or mucus membrane. Peptic ulcers are so common in industrialized nation that they virtually represent stigma of civilization.

Perforation is one of the most catastrophic complications of peptic ulcer. In spite of modern advances in surgical, anesthetic and ancillary facilities, it still assumes life-threatening dimensions. Prompt recognition of the condition is of paramount importance, as only by early diagnosis and treatment it is possible to reduce the still relatively high mortality.

Approximately 98-99% of peptic ulcers either in duodenum or in stomach in ration of 4:1. Duodenal ulcer is

the most common ulcer in the GI tract. Free perforation into the peritoneal cavity occurs in 2-3%. Perforation of duodenal ulcer is an emergency condition, which requires immediate surgical intervention. Peptic ulcers are remitting and relapsing lesions that are often diagnosed in middle aged to older adults (45 yrs. and above). 5-10% of patients have no recognizable prior ulcer symptoms and may appear after a period of weeks of months of active disease and heal with or without therapy. Thus it is difficult to express accurate data about frequency of active disease. The best estimate of peptic ulcer frequency is from autopsy studies and surveys of patients indicate a range of 6.14% for men and 2.6 for women. Perforation is one of the most dramatic complication of duodenal ulcer and perforated duodenal ulcer is most common perforation of upper GI tract. Ulcer that perforate mostly present on anterior aspect of first part of duodenum, rarely an ulcer is present in posterior wall and perforates in lesser sac and adjacent structures, most

often in pancreas, less commonly into liver, biliary tract or colon.

It is silient chronic ulcer that perforates specially in patients who are being treated wit steroids, usually symptoms of perforation occur with dramatic suddenness.

After perforation duodenal contents escape through the perforation into general peritoneal cavity resulting into the peritoneal reaction (Peritonism). Peritoneum reacts to this chemical irritation by secreting peritoneal perforation fluid copiously, which dilutes the contents, and this gives relief of pain for short time. This stage lasts for 3-6 hrs and is followed by diffused bacterial peritonitis.

Bacterial peritonitis develops late as there is sufficient acid from the stomach. If this condition is not treated immediately, the course is fatal. Patients die because of septicemia and peripheral vascular failure.

Peptic ulcer disease-including gastric and duodenal ulcers-has long been treated as a gastric acid secretion and disorder of the upper gastrointestinal tract. Despite the

discovery of the involvement of the microbe H. pylori in peptic ulcer disease and gastric cancer, prescribers have been slow to add antimicrobials to peptic ulcer disease therapy. In a 1995 British study, only 25% of gastroenterologists used anti- H. pylori therapy as a first-line treatment of duodenal ulcer patients. Most practitioners did not believe that the microbe was associated with gastric ulcers or gastric cancers. However, recent pharmacotherapeutic advances in treating peptic ulcer disease-histamine H2 antagonists, antisecretory compound, cytoprotective agents, and anti-infective therapy-having virtually eliminated the need for surgery in these patients.

EPIDEMIOLOGY AND ETIOLOGY

After its isolation from gastric mucosa in 1983, H. pylori (originally miscategorized as Campylobacter pylori) is a gram-negative, spiral-shaped bacterium capable of swimming or burrowing through gastric mucus. Once in the mucosal layer, where the pH approaches neutral, H. pylori

colonizes between the epithelial cell and the mucosal layer. It produces abundant urease, which hydrolyzes urea into ammonia and water. This causes localized inflammation, resulting in cytokine production.

The four to six sheathed flagella permit motility. The microbe uses urease to convert urea to ammonia and bicarbonate, tempering the acidic environment of the stomach in its immediate area.

H. pylori infections occur in some 50% of the elderly, with marked regional differences found in the United States- highest in northeast, lowest in South and West. African - Americans and Hispanics have a higher incidence that do whites, and lower levels of income, education, and socioeconomic status are associated with increased prevalence. The prevalence of H. pylori infection was reported as 43-78% in a 1995 review article that cited five prior studies. It notes that prospective serologic studies have found prevalence of 69-95% among patients with gastric cancer and 47-76% among control patients. Infected

individuals have a lifetime risk of 10-20% for developing peptic ulcer disease. Transmission likely occurs through fecal-oral contamination and the oral-oral route, and prevalence varies with water sources. A zoonotic link has been proposed based on isolation of similar organisms in commercially reared cats and infection of pet owners with gastric Helicobacter-like organisms. As many as 90% of duodenal ulcer disease patients test positive for H. pylori infection. While gastric acid and the other classic factors contributing to peptic ulcer disease are still believed to play a role, H. pylori is now considered the causative factor for peptic ulcer disease and its recurrence as well as gastric cancer.

The gold standard for diagnosis of H. pylori infection has been biopsy-obtained during endoscopy-followed by testing for urease and/or histologic staining with hematoxylin and eosin. However, no single test has yet emerged as definitive in daily clinical practice for several reasons.

Endoscopy-based techniques carry the risks inherent in that procedure and are expensive. Cultures – which would establish an H. pylori diagnosis beyond doubt-are difficult, expensive, and require seven days for results.

Histologic staining adds substantially to costs, but is viewed as worthwhile when added to a procedure as expensive as endoscopy. Urease testing of biopsy samples is common, inexpensive, and accurate. Among the noninvasive breath tests, serology is an option. It fails to differentiate between past and active infection, and thus it does not provide definitive support for initiation of therapy.

An FDA advisory committee has recommended the 14C-labeled urease breath tests for marketing, and agency action in imminent. The urease test is specific for current. H. pylori activity, provides results in 20 minutes, and may be used in physician offices. It is expected to provide an alternative to endoscopy in many patients.

The breath test involves patients' ingestion of a capsule containing 1μCi of [14C] urea (Tri-Med Specialties,

Charlottesville, Virginia). Twenty minutes later, the presence of radioactive carbon dioxide in the breath indicates H. pylori activity in the stomach.

Another noninvasive test now under study is an office-based serum test for anti-H. pylori antibodies (FlexSure HP, Smithkline Diagnostic, Islip, New York). Results on venipuncture samples are available in four minutes. Its usefulness is limited to patients' first diagnosis of infection, though, since it does not differentiate between active and past infection.

Three equally reasonable diagnosis and treatment protocols exist. A single, short-term trial of empiric antiulcer therapy using antisecretory agents, without proven H. pylori infection.

Definitive diagnostic evaluation, which should be aggressive in patients over 50 years old because of the link between H. pylori infection and gastric carcinoma.

Noninvasive testing for H. pylori followed by antibiotic therapy in positive subjects (this option includes dyspeptic patients without peptic ulcer disease).

EPIDEMIOLOGY

H. pylori infects more than half of the population world wide. Most individual infected are asymptomatic. The incidence is lower in development countries and there is an inverse relationship between prevalence and socioeconomic status. It is more prevalent in older adults. Transmission is probably from man to via faecal-oral or oral-oral routes. It has been demonstrated that iatrogenic spread can occur through contaminated endoscopes.

DIAGNOSIS

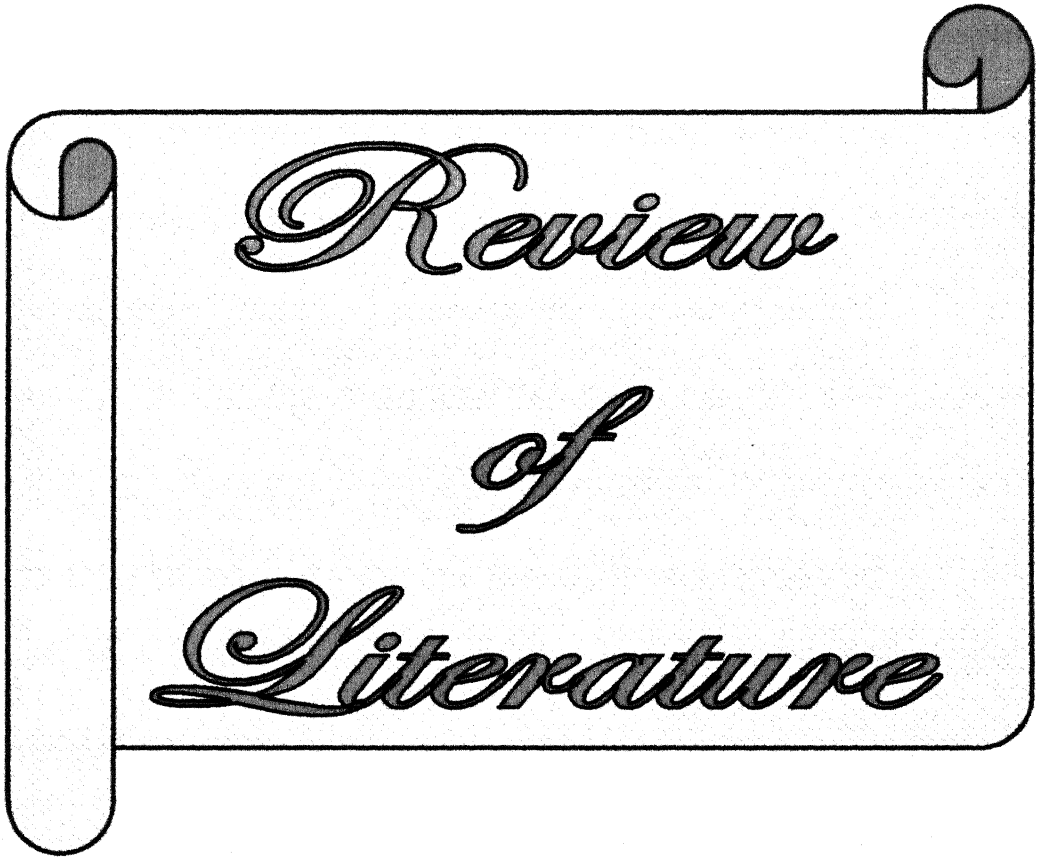
Tests for H. plyori are divided into invasive and non-invasive test depending on whether endoscopy is required. The serological tests measure specific H. pylori antibodies. A number of such tests are available commercially, the sensitivity and specificity of which vary considerably. Local

validation of the tests are desirable. Because the antibodies to H. pylori persist for a long time after H. pylori eradication, the serological tests are not recommended for documentation of success of H. pylori eradication. Another non-invasive test is the urea breath test. The patient is given either 13C or 14C-labeled urea to drink. The urease produced by H. pylori will metabolized the urea rapidly to ammonia and carbon dioxide which will be absorbed and then exhaled. The amount of labeled carbon in the expired air will be able to determine whether H. pylori is present, it is a very accurate method but is relatively expensive. It is reliable method to assess the H. pylori status after treatment.

The invasive tests require upper endoscopy and biopsy of the gastric mucosa. Histological identification of H. pylori has long been considered the gold standard of diagnostic tests. However, it is time consuming and expensive. Histology is generally unnecessary in patients in whom a biopsy urease test is positive. The biopsy urease

test is a colorimetric test based on the urease-producing ability of H. pylori. It is quick and accurate. When upper endoscopy is indicated, it is the test of first choice. Culture of biopsy specimens for H. pylori requires an experienced laboratory and is both time-consuming and expensive. It is only indicated when antimicrobial sensitivity testing is required.

Peptic ulcer disease Current scientific evidence points to a strong association between H. pylori and peptic ulcer disease. Cure of the infection results in a market reduction in ulcer recurrence. Permanent cure of the peptic ulcer can be achieved. Therefore it is recommended that all gastric and duodenal ulcer patients who are infected with H. pylori should be given eradication therapy whether the ulcer is active or in a remission. This also applies to patients with a history of ulcer bleeding or perforation. In complicated peptic ulcer disease, eradication of H. pylori should be confirmed. If available, the urea breath test is the ideal test to demonstrate H. pylori eradication.


Review
of
Literature

REVIEW OF LITERATURE

Peptic perforation is the most serious and important complication of gastroduodenal ulceration. The earliest mention of duodenal ulcer in the medical literature is in the London 'Medico-Chisurgical Transaction' of 1817. Mr. Travers there reports 2 cases of perforated duodenal ulcer.

In the second edition of Pathological and practical research on disease of the stomach by Dr. John Abercrombie five cases stored in literature are collected together.

The first clear description is usually attributed to cruveilhier (1829) whose name it bore for many years as the round ulcer of Cruveilhier but Methew Baillie pictured the lesion in a series of engravings published in 1979. The first paper specially devoted to this subject appeared in 1861, it dealt solely with perforating ulcer and notes were given of cases collected from literature.

In 1894 H.P. Dean recorded the first successful case of perforating ulcer treated by operation, LA Dun followed

him. The results of these two cases drew conspicuous attention to the subject, and other success quickly followed. Wair gave an excellent summary of the early cases, together with a critical review of the whole subject of perforating duodenal ulcer in his presidential address to the American Surgical Association.

Rosenow (1921) in Mayo Clinic produced peptic ulceration in rabbits by the intravenous injection of streptococci from human ulcer. Lvy (1920) produced similar results by injection of sterile broth. Braithwaite (1923) suggested a lymphatic infection. Seley and Colp (1941) have proved the presence of pathogens in peptic ulcer perforation.

Cushing's (1932) neurogenic theory in the causation of peptic ulcer is well documented. Mc Carrison (1924) has observed that the incidence of peptic ulcer is 50 times higher in South India than in North India. In 1936, it was pointed out by Mc Carrison, Somervell, and Orr that dietetic factors were of paramount importance in causation of peptic

ulcer. Diets poor in protein and vitamins A, B and C and fat have all been blamed.

Recently smoking has erupted up as an important etiological factor in the causation of peptic ulcer. In 1947, Jamieson et al studied the smoking habits of 437 cases of perforated peptic ulcer and concluded that heavy smoking was associated with severe symptoms. A carefully controlled study by Doll et al (1958) showed that smoking could be a factor in the production of peptic ulcer. Gastric secretion is stimulated with smoking has been proved by Gray 1930, Crohn (1938), Chrenfeld and Stutevart (1941) and Steigmenn, (1954).

Dodds and his associates (1934) produced chronic ulcer with perforation by oral and subcutaneous administration of pituitarin in rabbits, which produces mucosal ischemia by spasm. Mann and Williamson (1923) showed if the duodenal contents were diverted to the ileum and the jejunum exposed to undiluted gastric juice a typical

chronic peptic ulcer developed almost invariably, proving the importance of hyperacidity in the causation of peptic ulcer.

Genetic influences are important in predisposition to duodenal ulcer, which are as follows:

1) Duodenal ulcer is about three times more common in first-degree relations of ulcer patient that in general population.
2) A 50% concordance for duodenal ulcer has been observed in monozygotic twins as compared with 14% in dizygotic twins.
3) Individuals of blood group 'O' are about 37% more likely to develop duodenal ulcer than those with other blood groups.
4) An increase incidence of HLA b-5 antigens also has been identified in white males with duodenal ulcer.
5) The genetic trait with pepsinogen hypersecretion segregated as an autosomal dominant trait is hailed as a marker for predisposition to duodenal ulcers.

Duodenal ulcer is more frequent in patients with alcoholic cirrhosis, chronic renal failure and hyperparathyroidism. In general, duodenal ulcer patients have higher mean basal acid output and maximal acid output than do normal controls and significantly higher levels than present in patients with gastric ulcer.

There is evidence linking the recently isolated organism H. pylori[20]. H. pylori has been isolated from the gastric mucosa in 90% of patients with duodenal ulcers, 70% with gastric ulcers and 60% with non-ulcer dyspepsia (Marshal et al, 1985). The pathogenic role of H. pylori has yet to be confirmed, current evidence suggests that this organism is probably on of the several contributory factors in pathogenesis of peptic ulceration.

As yet the story is still unfolding. Even so, enough is now known to consider getting some of the fruits of a decade of research into practice – to cure peptic ulcer disease with antimicrobial therapy rather than put patients on expensive long term acid-suppressing therapies.

It is not intended here to give a definitive review of all the information that exists on H. pylori and associations with peptic ulcer disease. Rather, this section is designed to provide sufficient background information to familiarise the reader with the subject. There are a number of excellent reviews which describe various aspects of peptic ulcer disease, dyspepsia and H. pylori (Blaser, 1990; Soll, 1990; Petereson, 1991; Graham, 1993; Pope, 1994).

As usual, an excellent overview comes from the non-science literature. The Economist of March 5, 1994 produced a remarkably concise review of the H. pylori story with some punchy comment. It refers to an economic analysis by Ammon Sonnenberg of the Medical College of Wisconsin, demonstrating that a 15-year treatment of ulcer with current drugs would cost $11,500 per patients, to which could be added at least $17,500 if surgery is needed. Eradicating H. pylori would cost less than $1,000. Says Sonnenbery "From an economic perspective, antibiotic therapy is the treatment

of choice"; says the Economist "It also makes people healthier".

H. PYLORI

The presence of spiral – shaped micro – organism is stomach mucosa was described almost 100 years ago (quoted by Madan et al, 1988). Their presence was not really taken seriously until the late 1970s, when John Warren, a pathologist in Perth, Western Australia, noted the appearance of spiral bacteria overlaying gastric mucosa, and chiefly over inflamed tissue. Warren and Barry Marshall cultured these organisms in 1982 from 11 patients with gastritis; the story of the early part of the discovery of H. pylori is related by Marshall and is worth reading because of that (Marshall, 1989).

Originally called Campylobacter pyloridis. The name was changed to Camplyobacter pylori and then later to H. pylori as specific morphologic, structural and genetic features indicated that it should be placed in a new genus.

The organism is a motile, gram-negative, curved rod which is oxidase, catalase and urease positive.

Marshall and Warren were able to demonstrate a strong association between the presence of H. pylori and the finding of inflammation on gastric biopsy (Marshall & Warren, 1984). People who did not have gastritis did not have the organism, a finding confirmed in a number of studies (see below). Marshall elegantly fulfilled Koch's postulates for the role of H. pylori in antral gastritis with self administration of H. pylori, and also showed that it could be cured by use of antibiotics and bismuth salts.

EVIDENCE IMPLICATING H. PYLORI IN GASTRITIS AND PEPTIC ULCER

There are a number of pieces of evidence:-

Voluntary ingestion of H. pylori resulted in chronic gastritis inflammations (notably type B gastritis almost universally present in duodenal ulcer), not all types.

There is a systemic immune response to H. pylori infection. H. pylori antibodies diminish with effective

antimicrobial therapy. Clearance of gastric inflammation with bismuth salts (bismuth has antimicrobial properties).

ASSOCIATION OF H. PYLORI WITH EPIDEMIC GASTRITIS AND HYPOCHLORHYDRIA

Another compelling piece of evidence comes from the epidemiology of gastritis and H. pylori infection. The pattern of H. pylori acquisition with age is identical to that of gastritis. Serological tests for H. pylori infection (circulating IgG and IgA antibodies measured by immunological methods) show that H. pylori infection is low in children, but rises dramatically in the fifth and subsequent decades, and that more than half of the population over 50 years is infected. This seems to be due to a continuous risk of infection (Veldhuyzen van Zanten et al, 1994). The prevalence of chronic gastritis with age is given alongside the serology results below:-

H. PYLORI AND ULCERS

A further early finding was that infection with H. pylori was almost 100% in those patients with duodenal ulcers, and approached that figure in patients with gastric ulcers. Collected data from studies published up to 1990 are shown below (from Blaser, 1990).

People who have developed peptic ulcer are much more likely to have had H. pylori infection up to 10 years previously (Normura et al, 1994), and studies of twins n Sweden has shown that there is a considerable genetic component in susceptibility to infection (Malaty et al, 1994),

HOW DOES H. PYLORI CAUSE GASTRITIS AND ULCERS?

H. pylori are motile, even in the highly viscous mucus layer in which they live. This may allow the organisms to evade both gastric mtility and peristalsis, and to some extent gastric acidity also. The organism seems specifically to overlay gastric-type epithelial cells, whether in

the stomach or metaplastic in the duodenum; they will not overlay absortive-type duodenal cells, even when these are metaplastic in the stomach. Although it is motile, it also may adhere to the gastric mucosa through specific adhesion mechanisms.

The secretion of large amounts of urease result in any urea in the environment being converted into ammonia– with the result that the intense acidity of the stomach may be ameliorated in the Micro environment surrounding the bacterium. The Michaelis constant of H. pylori urease is 0.4 mm. making it one of the lowest known for this enzyme, and allowing significant conversion of urea to ammonia at very low urea concentrations and, therefore, to work efficiently in the stomach.

About 50% of H. pylori strains produce cytotoxins (Crabtree et al, 1991b), of which some have been specifically linked to active gastritis and peptic ulceration. The strains isolated from patients with the most severe disease tend to be more likely to secrete these cytotoxins

than strains isolated from asymptomatic patients. These cytotoxins can cause local inflammation, though other secretions by organism, such as proteases and phospholipases, can attack and damage mucosal cell membrances. Weakening the gastric - mucosal barrier permits back - diffusion of hydrogen ions resulting in further tissue injury, as well as causing local immune responses to the organism.

There is also evidence that H. pylori infection is responsible for reducing the levels of ascorbic acid in the gastric juice; levels in infected patients were only 25% of those in non-infected subjects (Banerjee et al, 1994). Moreover, eradication of H. pylori resulted in a large increase in gastric juice ascorbate. The reversible lowering of gastric juice ascorbate may predispose to gastric cancer and peptic ulceration (Banerjee et al, 1994).

It is entirely likely that assays could be made available which detected antibody response to the aggressive strains of H. pylori or their associated damaging

cytotoxins. Such a development would allow for a much more simple therapeutic approach – if a test for such an aggressive strain proved positive in symptomatic or asymptomatic individuals, eradication would be a sensible first course of action.

METHODS OF DIAGNOSING H. PYLORI INFECTION

There are several methods which can be used to diagnose whether a patient is infected with H. pylori. They differ in being invasive or non-invasive. Simple or difficult, cheap or expensive. Though far from an exhaustive coverage, the main points of each method are given below.

INVASIVE METHODS

CULTURE

H. pylori can be cultured only when a specimen containing the pathogen has been obtained, and in his case that means obtaining a biopsy specimen at endoscopy. Methods of culture vary, but in general they involve homogenisng the biopsy specimen and culturing the

homogenate on a variety of specialised agar plates at elevated temperatures for at lease seven days.

Culture is generally regarded as the 'gold standard' for detecting a bacterium. For H. pylori, however, the success of the technique depends on local technique and access to facilities, and can be regarded as being no more than 60 – 90% sensitive, though being 100% specific; the cost of each testis high (DeCross & Puera, 1992; Perez et al, 1988).

HISTOLOGY

Histological examination of tissue biopsy samples (usually four, taken from different parts of the stomach lining) permits detection of the bacterium together with evaluation of tissue damage. Most infection can be detected with haematoxylin & eosin H&E results are not conclusive.

The sensitivity of Wright-Giemsa and Brown0Hopps stains has been shown to be 100%, compared with H&E (Madan et al, 1988), though histological detection of the organism has generally been considered to have lower

sensitivity at 80 - 95% with 100% specificity. The need for a number of biopsy specimens to be examined by experienced pathologist renders histology expensive, and it requires an invasive procedure.

CLO TESTING

The CLO test is for Campylobacter-like organisms. At the time of endoscopy and biopsy, a pinch of tissue is removed and placed in a test solution containing urea, a pH colour reagent and a bacteriostatic agent. The presence of urease from H. pylori results in hydrolysis of neutral urea to alkaline ammonia, together with a pH change and a change in colour (usually from yellow to red).

In infected tissues the change occurs within about one hour, so that the results of the CLO test are often available while the patient is still at the endoscopy unit, meaning that therapy decisions can be made immediately. Though the test itself is inexpensive, it still requires an invasive procedure to obtain the sample. It has 90-95%

sensitivity and high specificity, and the overall cost is moderate.

NON-INVASIVE TESTING

BREATH TESTING

Urea breath testing is non-invasive, and a specific indicator of H. pylori infection (Atherton & Spiller, 1994). The procedure requires a patient to attend a centre fasting, to eat a standard meal and then ingest urea labeled with C-14 or C-13. The presence of large amounts of H. pylori urease results in the production of labeled carbon di-oxide, which is absorbed into the blood and excreted in the breath. Samples of breath are collected before and some time after the ingestion of labeled urea and the amount of labeled carbon di-oxide measured by mass spectrometry or radioactive counting.

While quite specific, few detection systems are readily available, and they do have a significant capital cost.

Breath samples can be sent by post to measuring centres, though this involves a necessary delay before results are available. Breath testing is both sensitive (at least 95%) and specific (at least 98%) with a moderate cost.

Breath testing has the important advantage of being both non-invasive, and being able to confirm H. pylori eradication about one month or so after treatment has ended, should that be necessary.

ANTIBODY MEASUREMENT

Patients infected with H. pylori have immunoglobulin antibodies to the organism. Tests for the detection of antibodies to H. pylori circulating in blood, or found in saliva, have excellent sensitivity and specificity of above 95% and are cheap and simple compared with invasive techniques (DeCross (Puera, 1992). They can give very quick results even within minutes of the first consultation, and are the only tests which are not likely to give false negative results in patients who have taken antibiotics, bismuth compounds

or omeprazole in the recent past (NIH Consensus Conference, 1994).

Because there are different strains of H. pylori, antigen for antibody manufacture is generally prepared by using preparations from several different strains. Antibody assays in blood have measured IgG and IgA antibodies which have been shown to be specific for H. pylori and not other gram-negative organisms (Perez-Perez et al, 1988). Where both IgG and IgA assays have been compared with other testing methods, like culture and/or histoglogy, IgG assays tend to have slightly high sensitivity and specificity, and so anti-IgG methods tend to be favoured (Perez-Perez et al, 1988; Glassman et al, 1990; Crabtree et al 1991a).

The commercially available assays are of two sorts: either microtitre-plate assays for use in a laboratory, or near-patient testing devices. Both types of assay usually have a cut-off value set with control sera so that they differentiate patients with H. pylori infection from those who do not, rather than quantify the concentration or circulating

anti-H. pylori immunoglobulin. Laboratory based microtitre assays (Crabtree et al, 1991a) and near-patient testing devices (Pronovost et al, 1994) perform equally well compared with standard techniques.

Test for antibodies to H. pylori in saliva are equally effective as those for antibody in serum (Patel et al, 0994). In saliva IgG immunoglobulins must be measured, as measuring IgA antibodies does not distinguish positive from negative cases.

Antibody tests have high sensitivity and specificity when compared with other methods. They also have the advantage of being non-invasive, and near-patient versions are available which can produce results from a small finger prick of blood within a few minutes. The costs of antibody tests (bedside or laboratory) are much lower than any other methods.

At least one commentator has suggested that for H. pylori infection, serology testing may be the "gold standard" (Blaser, 1990). Essentially, every person who gastric biopsy

can be showed to harhour H. pylori has evidence of a systemic humoral immune response. Those in whom the organism cannot be detected by the other methods have a low false positive rate by serology. However, gastritis can be a patchy phenomenon and histologic biopsy and culture assess only a small area of the stomach, while serology in essence assays the entire stomach. "False-positive" serology may well, infact, reflect falsely negative biopsy results.

QUANTITATION OF ANTIBODY TESTS

Knowing how much antibody was present in the blood has not generally been thought to be helpful. Very high concentrations have been found in infected patients who also have gastric cancer (Forman et al, 1991), and more recently Nomura and colleagues (1994) found that there was a higher degree of association between H. pylori infection with higher levels of circulating antibodies. The extent of the elevation in this study was much lower than that seen by Forman and colleagues for gastric cancer.

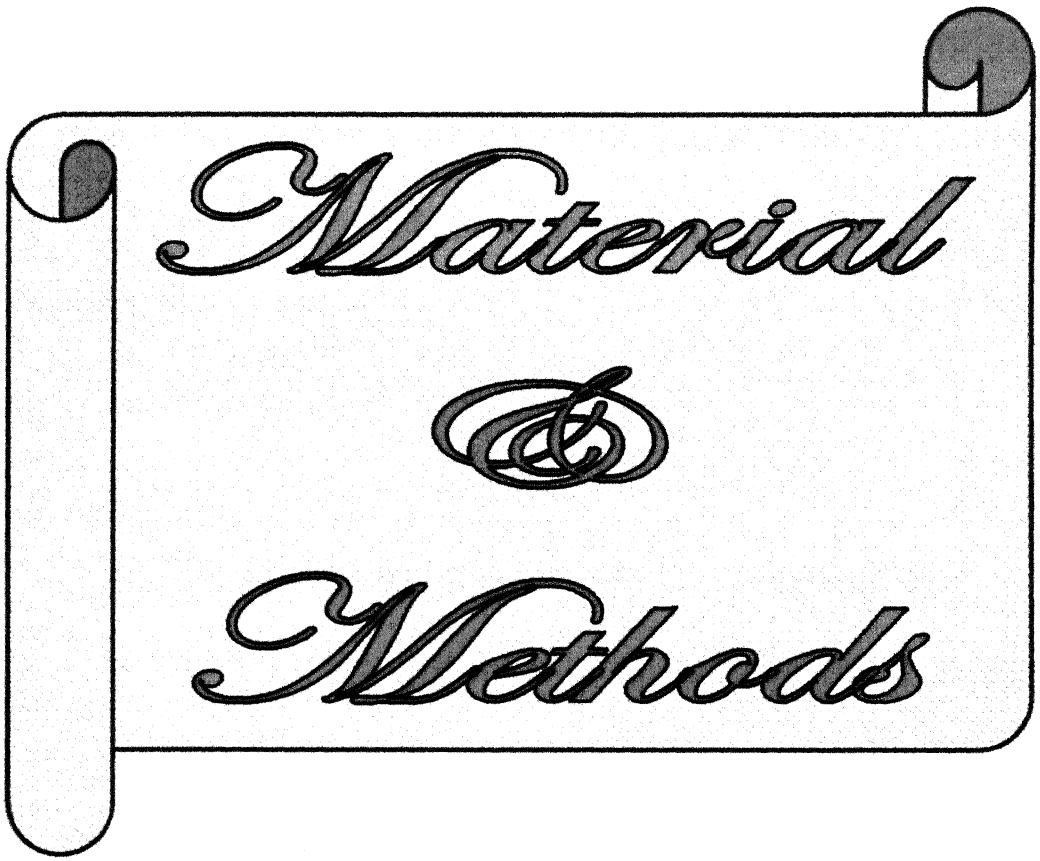
Almost all studies have concentrated on demonstrating the presence of antibodies to H. pylori as a means of diagnosis of infection. Systematic attempts to correlated levels of antibody to particular disease states have not been conducted. It is interesting to speculate that tests which discriminate actual circulating concentrations of antibodies to H. pylori might increase significantly the diagnostic yield for both peptic ulcer disease and gastric cancer, thus making screening a viable option for these diseases.

ANTIBODY TESTING AFTER H. PYLORI ERADICATION

Titres of IgG and IgA in serum fall relatively slowly after H. pylori has been successfully eradicated. Thus six weeks after eradication titres fall by about 20-30%, but by six months, about 97% of patient have titres reduced by 50% or more from pre-treatment levels (Kosunen et al, 1992). Because of this slow reduction in antibody titres after successful eradication, serology testing is not generally useful in confirming the success of eradication within a few

weeks of treatment; urea breath tests and histology or culture after repeat endoscopy can make that confirmation, if needed. However, since H. pylori reinfection or regrowth can take place within the first six months after treatment, waiting at least six months before retesting may be a better option.

However, there is one report, albeit of a preliminary nature, which indicates that in saliva, antibody titres to particular H. pylori membrane antigen fall much more rapidly (Clancy et al,1993). In a small number of patients it was showed that 83% had falls in salivary antibody titres of more than 50% within one month of successful eradication therapy. As an indicator of successful treatment, this is similar to standard methods for monitoring elimination.


Material
&
Methods

MATERIAL AND METHODS

The present study was conducted on patients with clinical diagnosis of perforation of chronic peptic duodenal ulcer presenting emergency ward of M.L.B. Medical College, Jhansi in Department of Surgery from May 2000 to April 2004 (retrospective study) and May 2004 to April 2005 (prospective study).

Following plan of work was followed :-

1. Preoperative work up (Clinical and biochemical).

 A. Evaluation and analysis of symptoms in order to find out duration of perforation and incidence of each symptoms :-

 - Pain in abdomen.
 - Fever.
 - Absolute constipation.
 - Vomiting.
 - Distension of abdomen.

B. Past history in order to find out high risk cases and incidence of acid peptic disease.

- Diabetes Mellitus.
- Hypertension.
- Pulmonary disease.
- Drug intake like NSAIDS & steroids.
- History suggestive of acid peptic disease.

C. Presence / absence of psychological factors (stress, anxiety).

D. Family history.

E. General examination and systematic examination in order to assess general condition of patient suitable for anesthesia and surgery.

- General condition.
- Blood pressure (mm Hg).
- Pulse rate (per min.).
- Respiratory rate (per min.).

- Anemia.
- Jaundice
- Urine output.
- Cardiovascular examination.
- Respiratory examination.

F. Local examination of abdomen to make clinical diagnosis and analysis of signs in order to evaluate incidence of each sign :-

- Board like rigidity.
- Tenderness.
- Guarding.
- Distension of abdomen.
- Masking of liver dullness.

G. Investigations

- Hemogram – Hb, TLC, DLC.
- Renal functions:
 a) B. Urea (mg%).
 b) S. Creatinine (mg%).

- S. Electrolytes.
 - c) S. Na^+ (Meq/L).
 - d) S. K^+ (Meq/L).
- Radiology.
- Plain X-ray abdomen erect A.P. view including both lobes of diaphragm.
- USG findings.

All patients were resuscitated with :-

- Intravenous fluids.
- Appropriate antibiotics.
- Nasogastric decompression by Ryles tube.
- Catheterization.

2. Pre-operative work up :-

All of the patients were operated under general anesthesia and preferable incision was midline.

During operation following points were recorded.

1. Size of perforation diameter.
2. Site of perforation.

3. Surrounding wall of duodenum.

4. condition of omentum.

5. Any additional finding on exploration.

The peritoneal soiling was cleared by peritoneal lavage and lavage fluid was suctioned out, the definitive procedure then performed.

3. Post operative work up :-

- IV Fluids.
- IV antibiotics.
- Active Ryles tube suction.
- Assessment of vitals viz. Blood pressure, Pulse rate, Respiratory rate, Urine output.
- Assessment of abdomen to see board like rigidity, guarding.

Postoperative patients were kept nil orally along with Ryles tube aspiration till bowel sounds were heard and flatus appreciated by the patient. Drains were taken out according to the amount of drainage. Ryles tube was removed after

3-5 days. Patients were called up after 7 days, 15 days, 2 months and 6 months.

Upper GI endoscopy to take the antral mucosa biopsy, for biopsy ureas test when ever possible, in the post operative period.

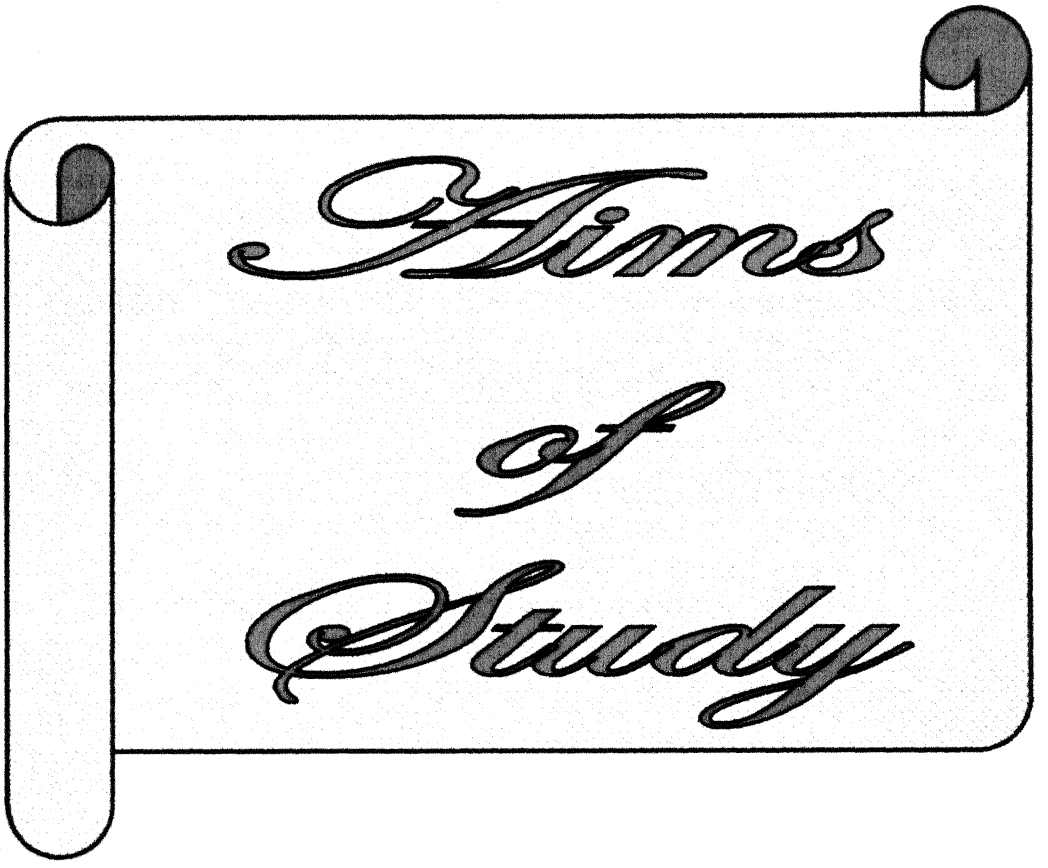
In all the patients an upper G.I endoscopy was performed in variable post of period from 3 – 7 day and two specimens were obtained by biopsy foreceps from gastric antral mucosa.

Both the specimens were immediately put in two separate test tube. Containing rapid ureas test solution.

Both the test tube were kept at room temperature and the result in form of colour changes read within 40 hrs.

Results are read as positive when both the test tube shown colour changes within 48 hrs.

Point were followed for follow up Upper G.E. endoscopy and Antral mucosa biopsy within six months.

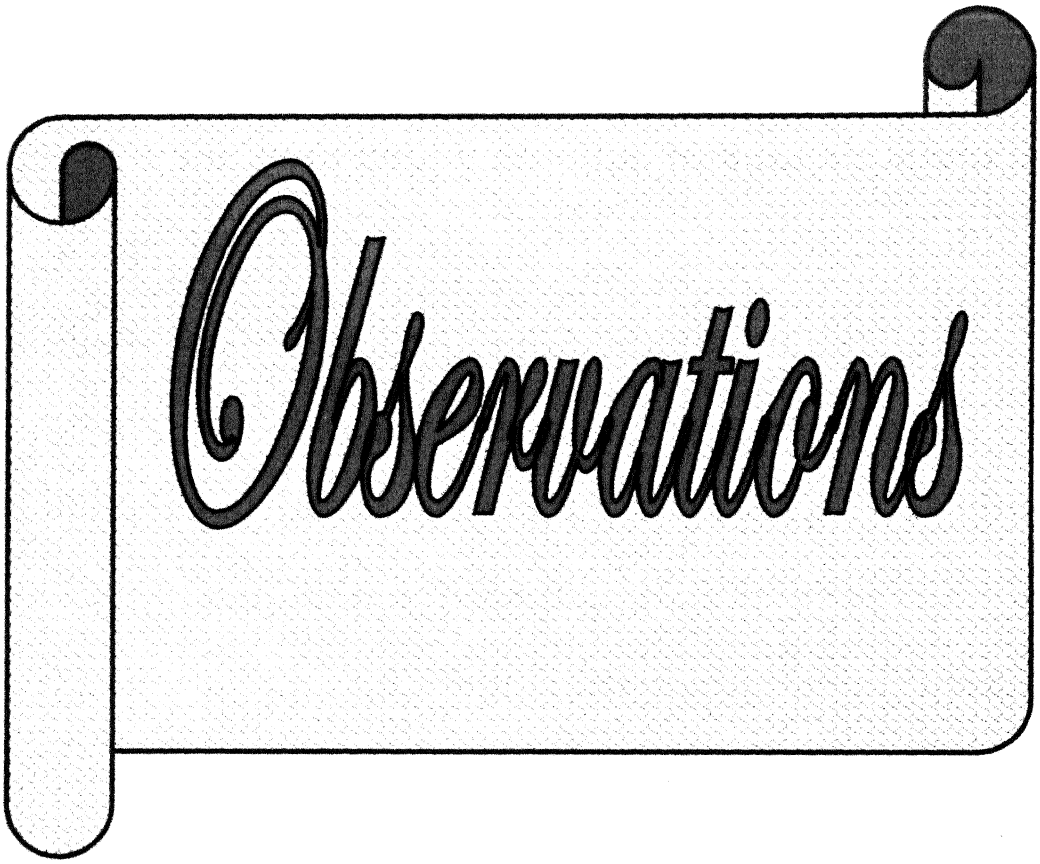

Aims
of
Study

AIMS OF STUDY

- To evaluated the prevalence of H. pylori in perforated peptic ulcer by obtaining antral mucosal biopsy with use Endoscopy in post operative period; whenever possible; by using biopsy urease test.
- Possible cause of ulceration / precipitation of Perforation.

OTHER PARAMETERS WILL BE STUDIED.

- Age distribution of peptic perforation.
- Sex distribution of H. Pylori in peptic perforation.
- Associated disease – TB, IHD, ARF, DM, HTN.
- Size of perforation in millimeters.


Observations

OBSERVATIONS

The present study has been carried out on 25 patients of confirmed peptic perforations cases per operatively from a period of 2005 to September 2006 in General Surgery Department of M.L.B Medical College and Hospitals, Jhansi, India.

All the patients were operated on in emergency operation theater and in post operative period all these patients were go through Upper G.I Endoscopy in variable post operative period from 5 to 10 days.

During endoscopy two specimens of GASTRIC ANTRAL MUCOSA were taken immediately put into two test tubes containing rapid urease solution and kept in room temperature and results were read with in 48 hrs, produced by color change of solution in test tubes

OTHER VARIABLE STUDIED IN THIS STUDY ARE-

1) Age distribution of perforation.

2) Sex distribution of perforation.

3) Associated factors – cigarette smoking, alcohol, life style, education status, food habit, economic status, occupation.

4) Size of the perforation.

5) Associated disease – hypertension, diabetes mellitus, ischimic heart disease, Tuberculosis, CRF.

6) Proportion of gastric and Duodenal perforation.

After study following fact were drawn.

AGE WISE DISTRIBUTION

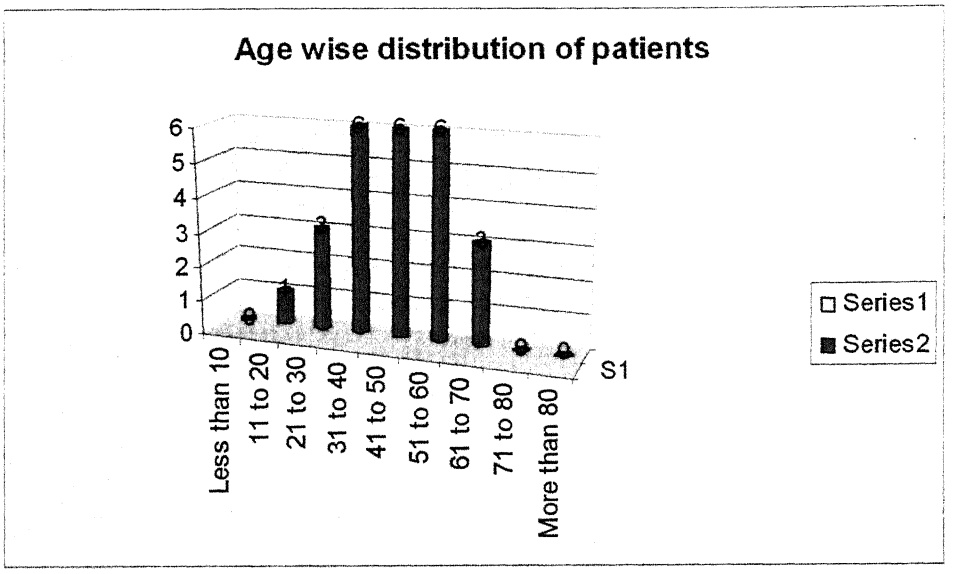
TABLE NO. 1

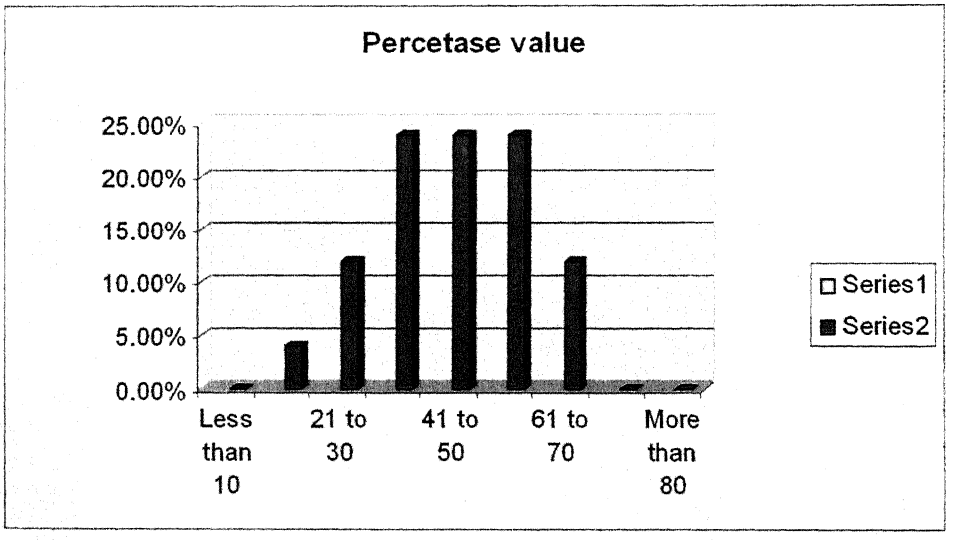
AGE (years)	DU	GU
Up to 10	0	0
11-20	1	0
21-30	3	0
31-40	6	0
41-50	6	0
50-61	6	0
61-70	3	0
71-80	0	0
More then 80	0	0
TOTAL	25	

Age range in present study was 19-67years. The youngest patient was a 19 years old boy and oldest patient was a 67years old man.

The maximum number of patient 18 out of 25 (72%) were in the age group of 31-60 years.

There was no case of GU in present study.


Age wise distribution of patients
6
5
4
3
2
1
0
Less than 10
11 to 20
21 to 30
31 to 40
41 to 50
51 to 60
61 to 70
71 to 80
More than 80
S1
Series1
Series2

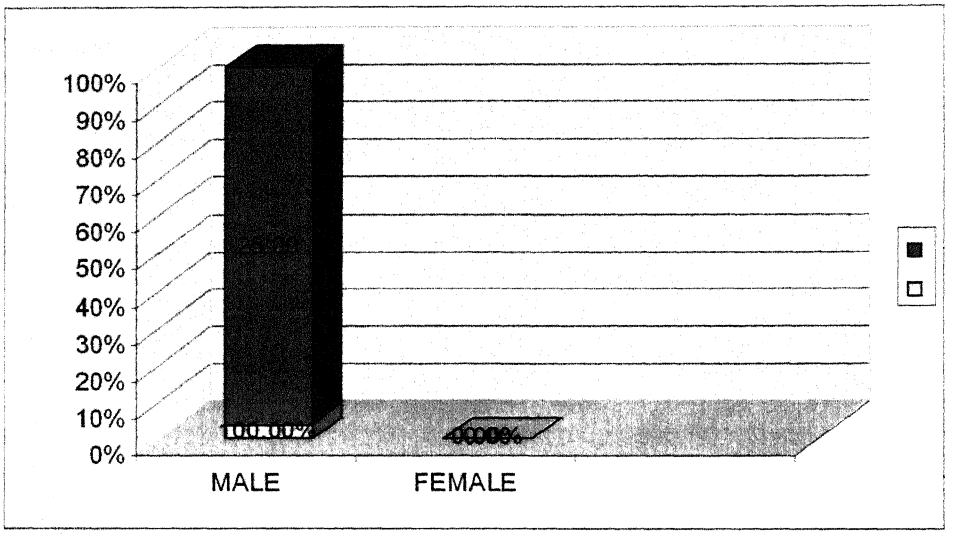

Percetase value
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
Less than 10
21 to 30
41 to 50
61 to 70
More than 80
Series1
Series2

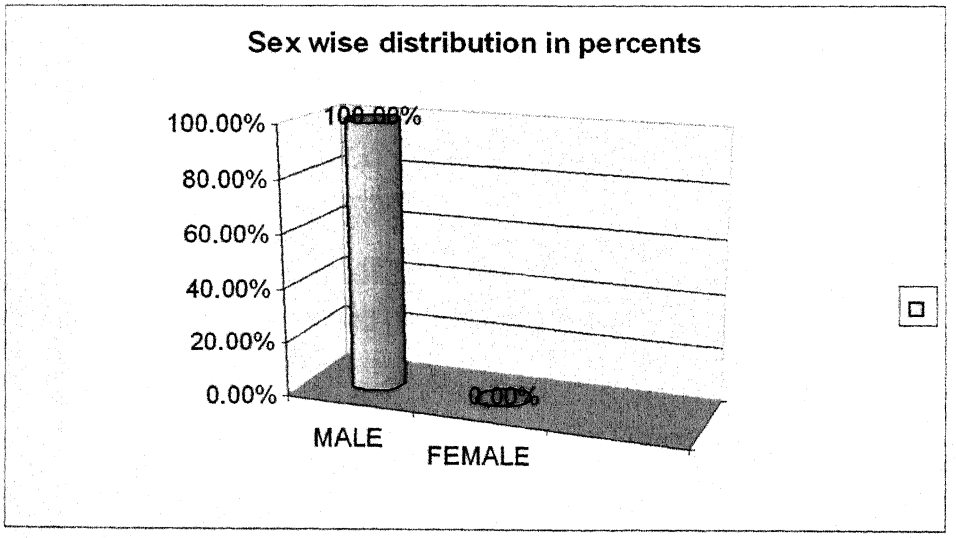
SEX WISE DISTRIBUTION

TABLE NO. 2

All the patient in study were male (100%).

Sex	DU	GU
Male	25	0
Female	0	0
Total	25	0





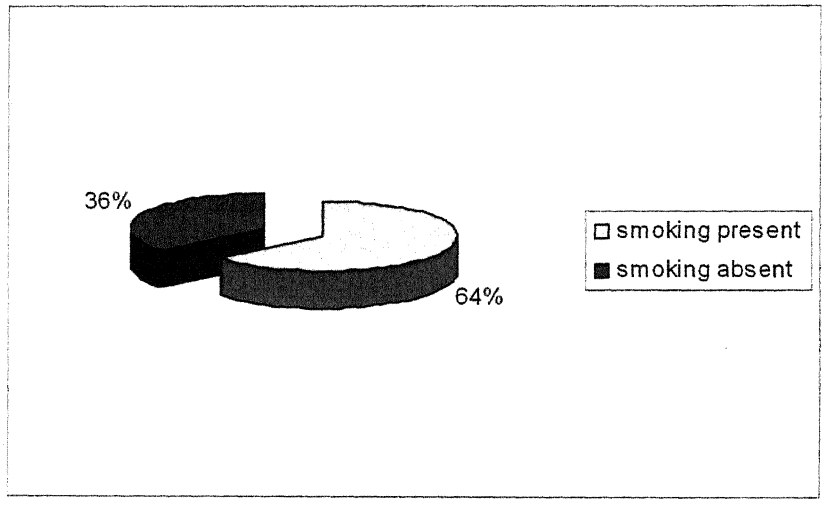
PATIENTS WITH CIGARETTE SMOKING

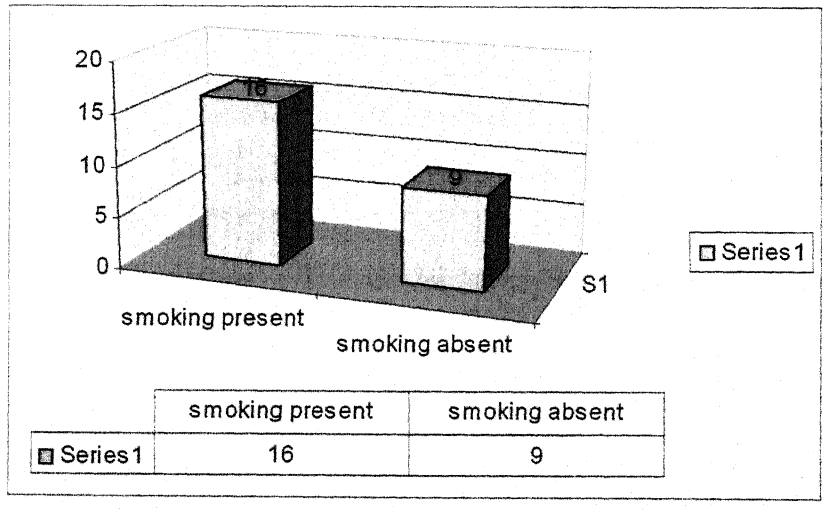
TABLE NO. 3

Cigarette smoking	Present	Absent
	16	09

Out of 25 patients, 16 patients were chronic smoker for 5 to 25 years, they were smoking 5 to 30 beeri/day

9 patients were non smoker, and they do not smoke.



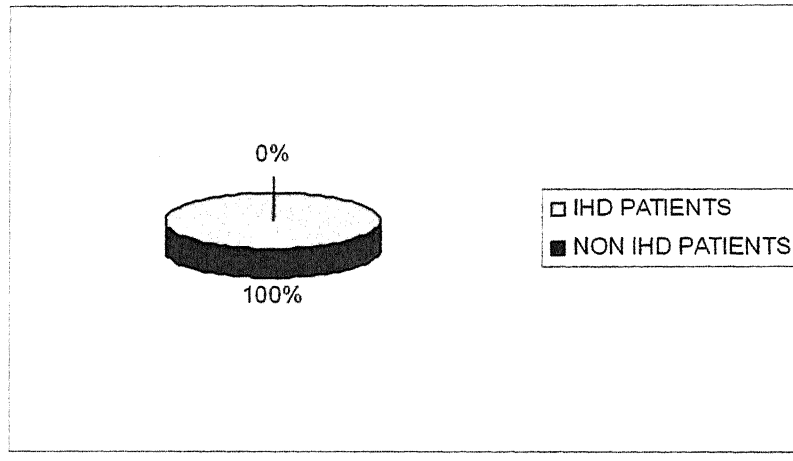


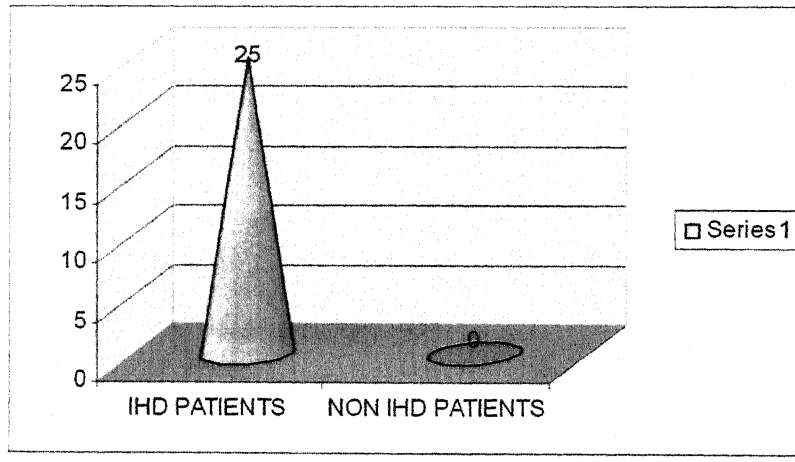
PATIENTS WITH IHD

TABLE NO. 4

Disease	Present	Absent
IHD	0	25

In this study no patient have IHD all the patient have no heart disease, decided by pre op and post op ECG.



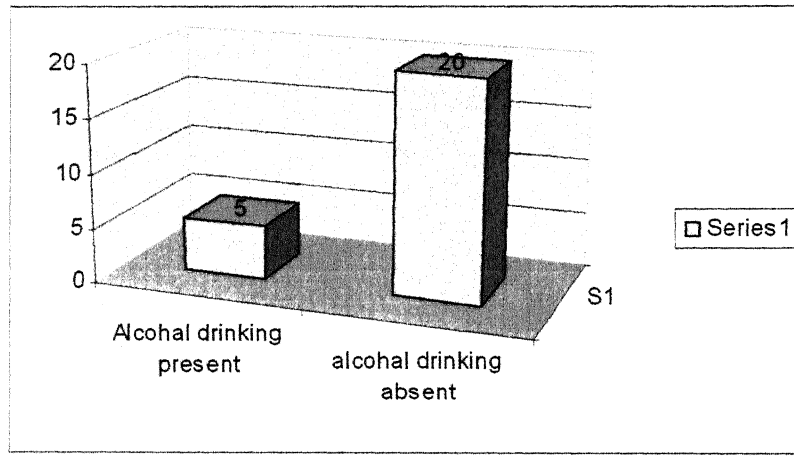


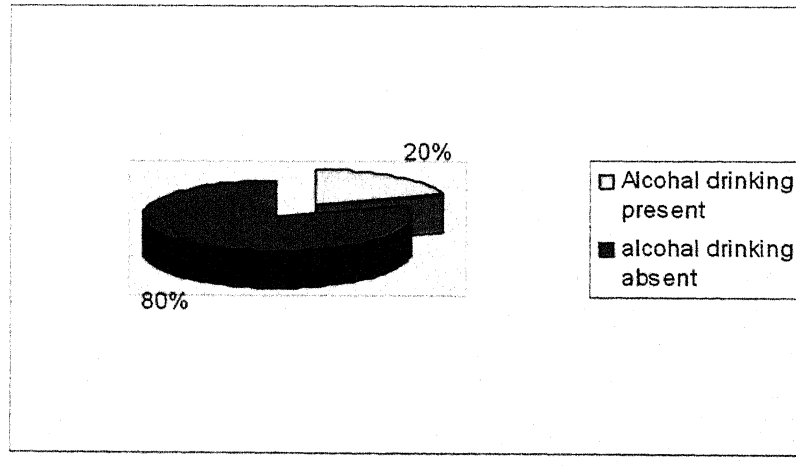
PATIENTS WITH ALCOHAL DRINKING

TABLE NO. 5

ALCOHAL DRINKING	PRESENT	ABSENT
	05	20

Out of 25 patient 5 (20%) patient were drinker and 2 (08%) of them are chronic drinker for a period of 10 to 20 years. 3 (12%) patients were occasional drinker. 20 (80%) patient were non drinker.



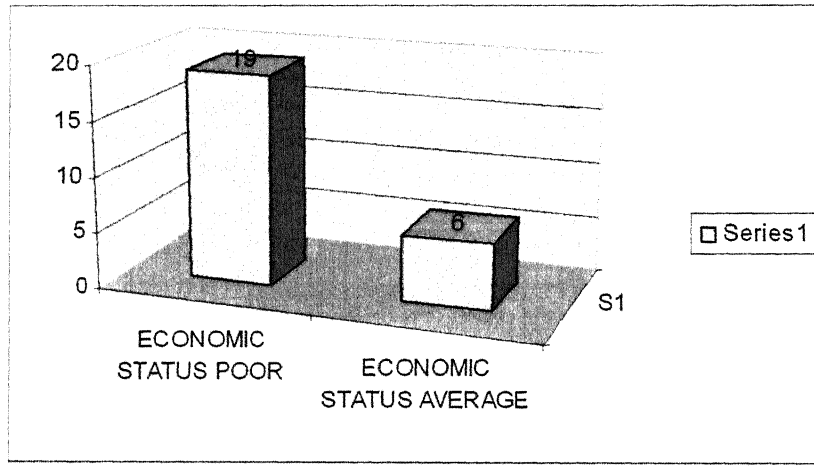


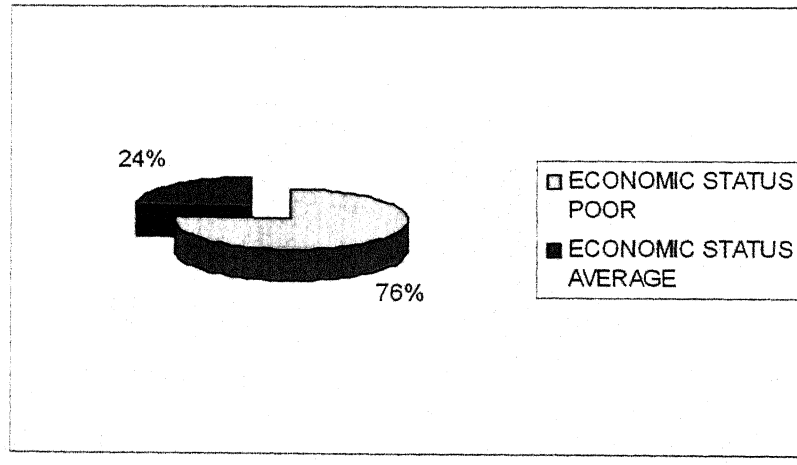
PATIENTS WITH DIFFERENT ECONOMIC STATUS

TABLE NO. 6

ECONOMIC STATUS	POOR	AVERAGE
	19	06

Out of 25 patient 19 (76%) patients were belonging to poor economic status. While 06 (24%) patients were from average family.



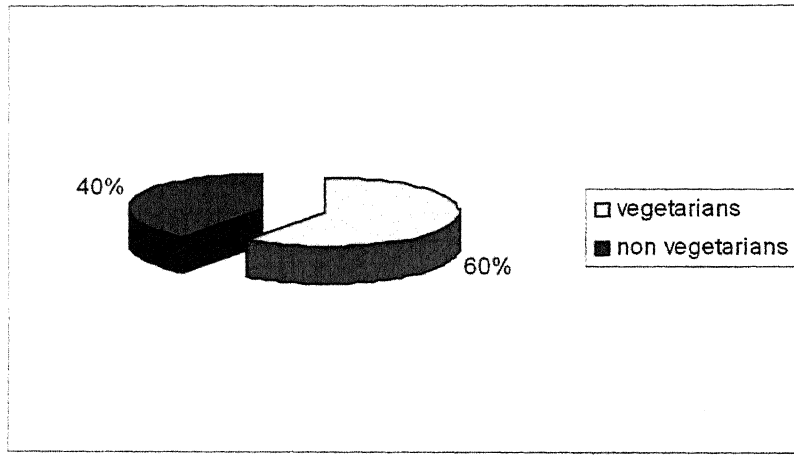


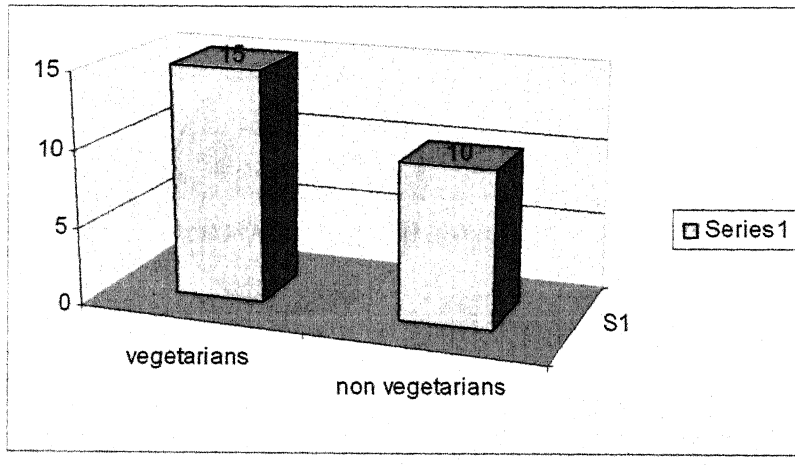
PATIENTS WITH DIFFERENT FOOD HABITS

TABLE NO. 7

FOOD HABIT	VEG	NON VEG
	15	10

In this study 15 (60%) patient out of 25 patients were vegetarian and 10 (40%) out of 25 patient were non vegetarian.



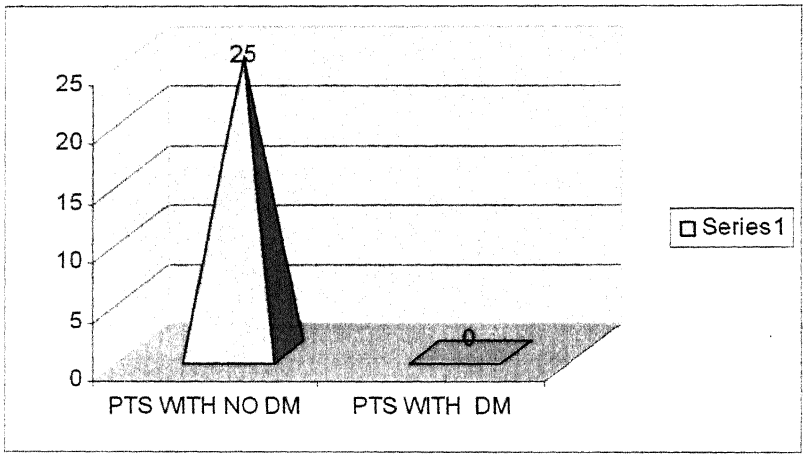


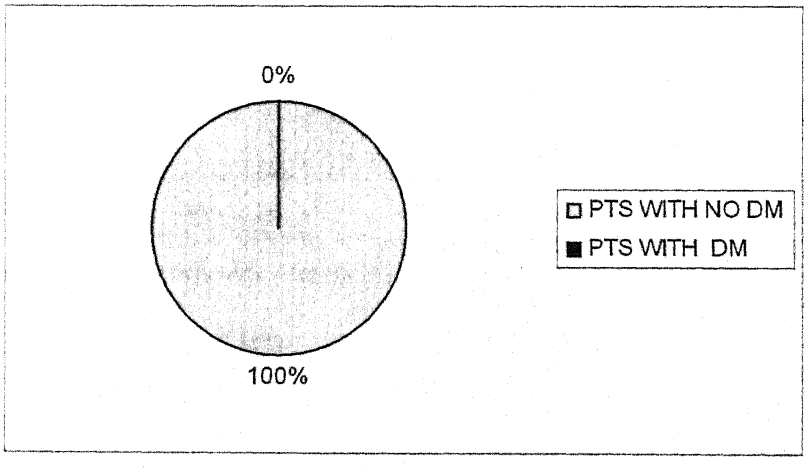
PATIENTS WITH DM

TABLE NO. 8

Disease	Present	Absent
DM	0	25

In this study no patient was suffering from DM, All the patient were non diabetic.



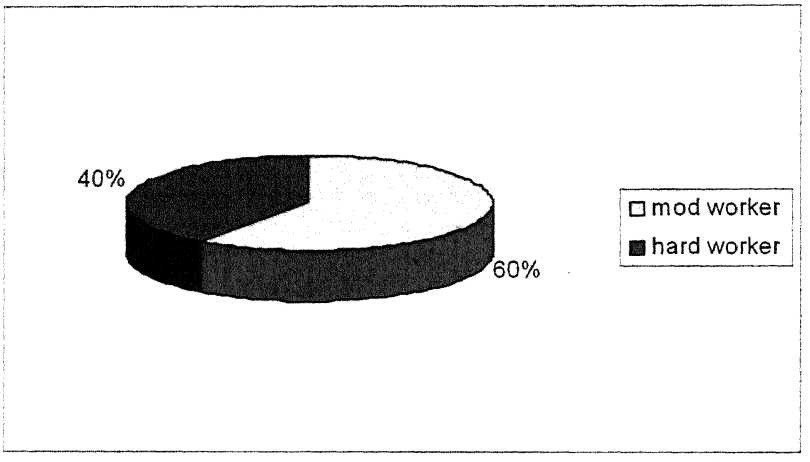


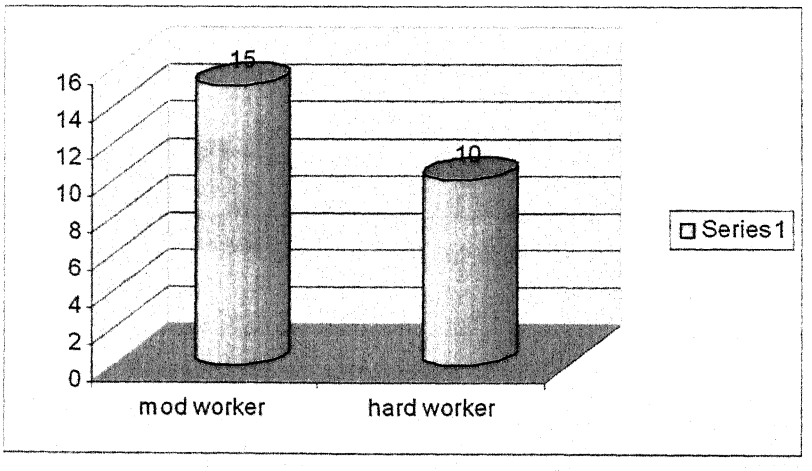
PATIENTS WITH DIFFERENT LIFE STYLE

TABLE NO. 9

LIFE STYLE	MOD WORKER	HARD WORKER
	15	10

In this study 15(60%) patients were mod worker and 10(40%) out of 25 were hard worker.



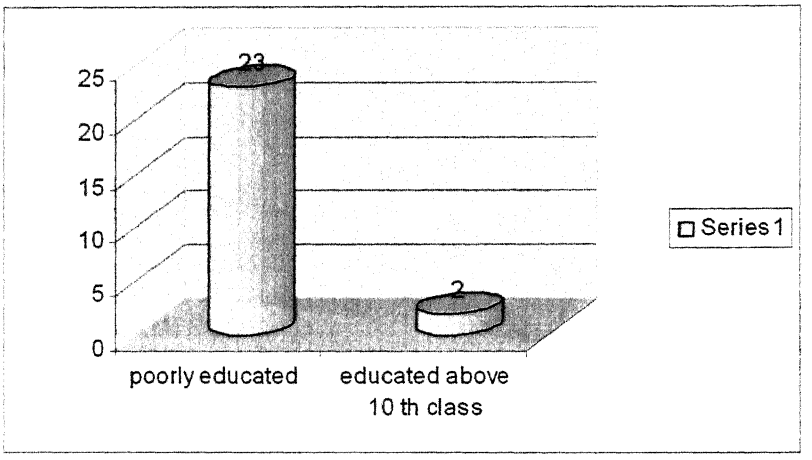


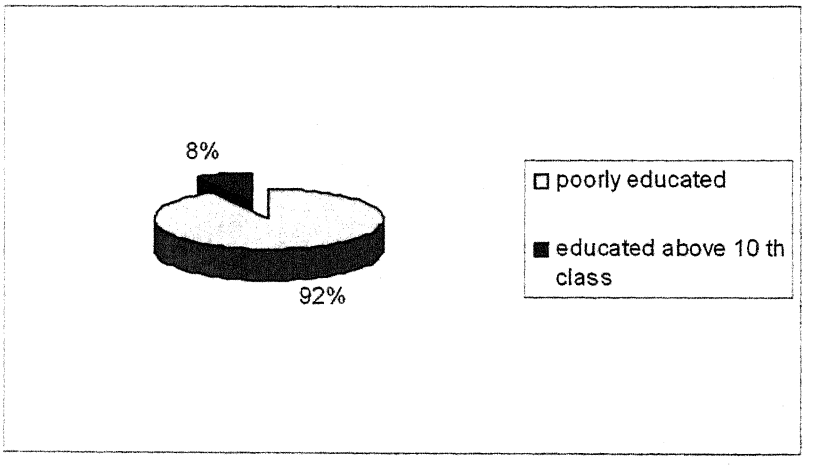
PATIENTS WITH DIFFERENT EDUCATION STATUS

TABLE NO. 10

EDUCATION STATUS	POOR	ABOVE 10th
	23	02

In this study out of 25 patients only 02 patients were educated above 10th class, rest 23 patients were poorly educated.



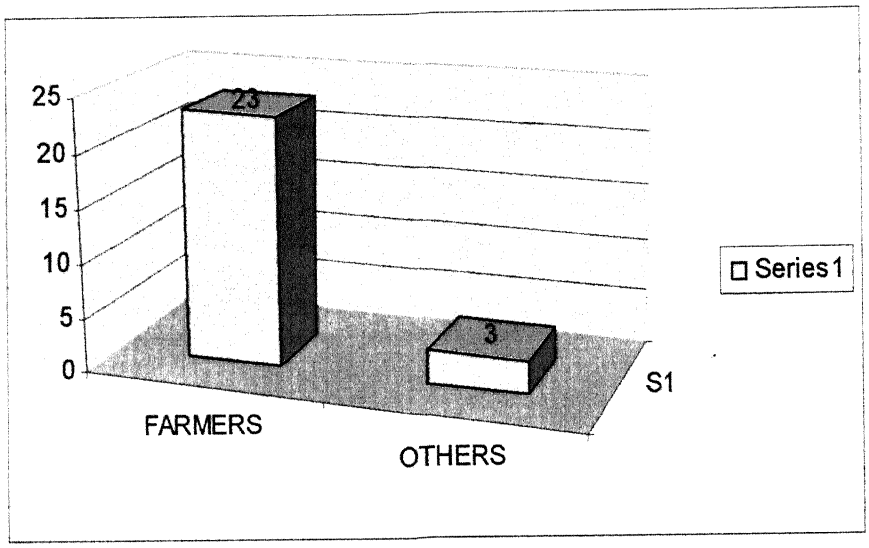


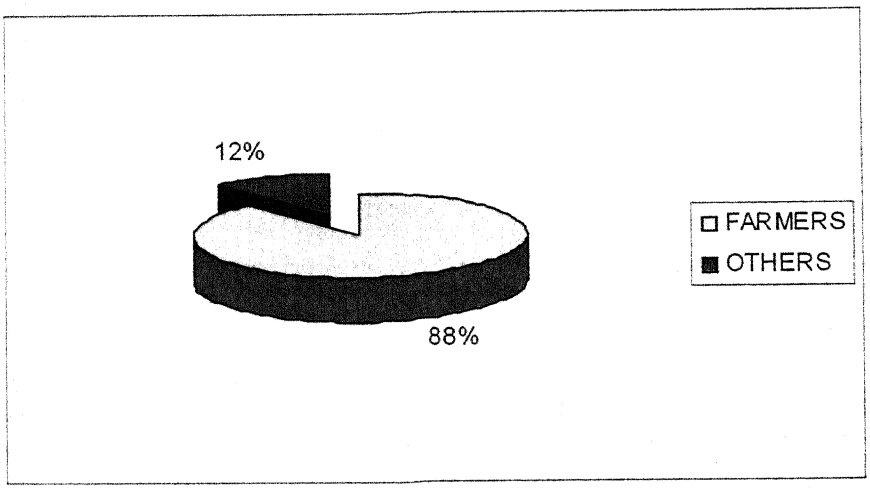
PATIENTS WITH DIFFERENT OCCUPATION

TABLE NO. 11

OCCUPATION	FARMERS	OTHERS
	22	03

Out of 25 patients 22 were farmer by occupation and rest 03 were from other occupation.



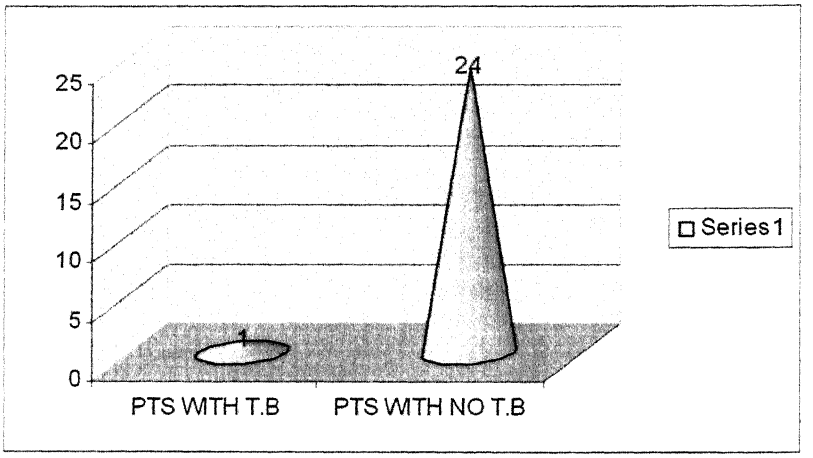


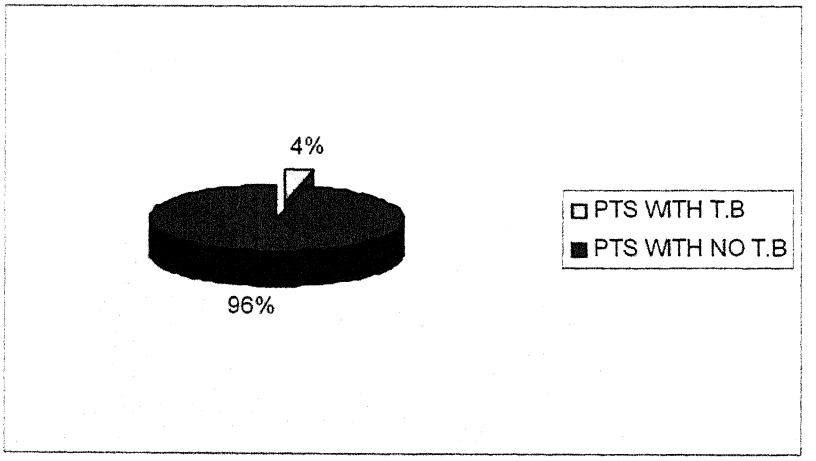
PATIENTS WITH TUBERCULOSIS

TABLE NO. 12

TUBERCULOSIS	PATIENTS WITH T.B	PATIENTS WITH NO. T.B
	01	24

There was only one patient suffering from tuberculosis, rest were non tubercular.



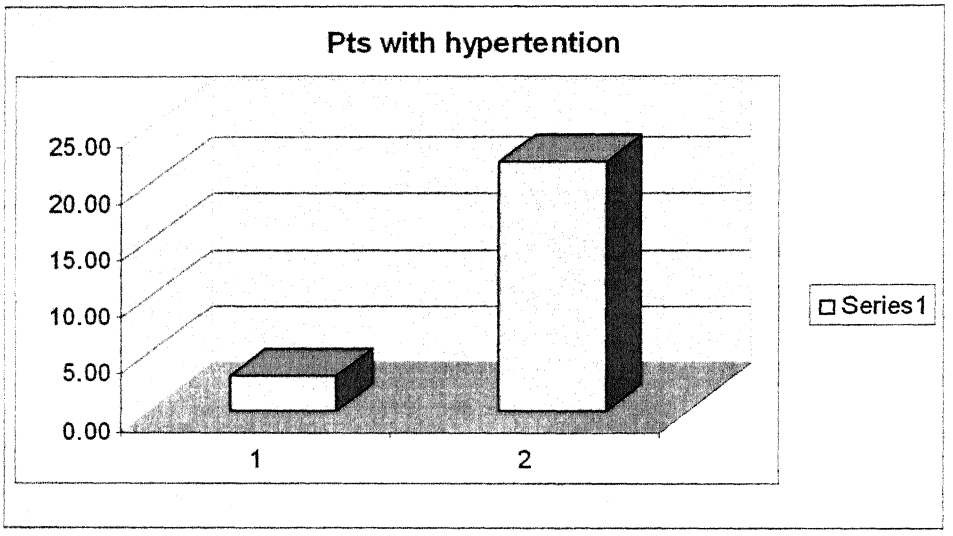


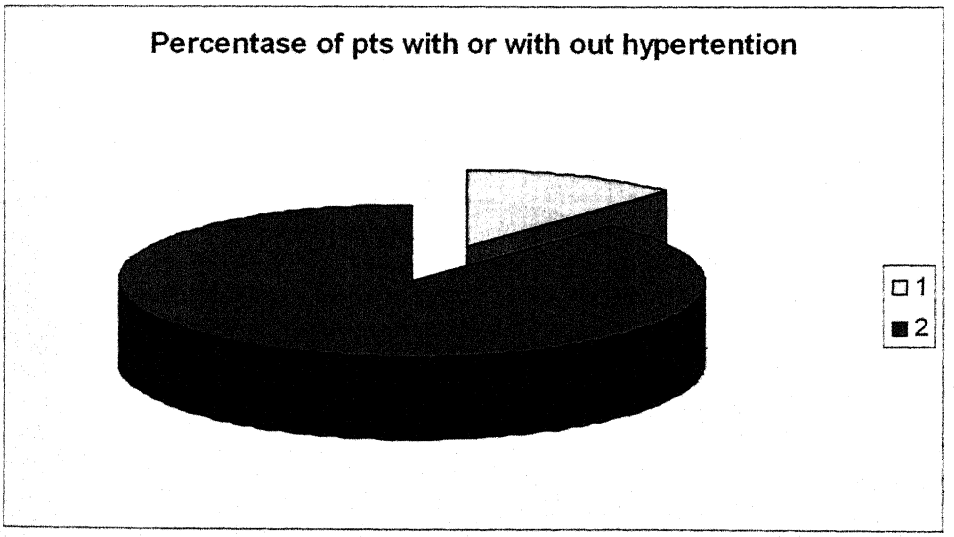
PATIENTS WITH HTN

TABLE NO. 13

Disease	Present	Absent
HTN	3	22

In this study 3(12%) patient were hypertensive and 22 (88%) patient were normotensive.



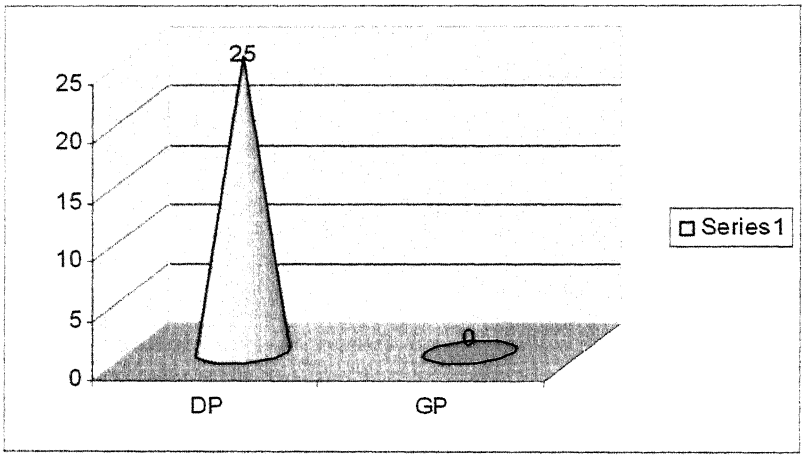


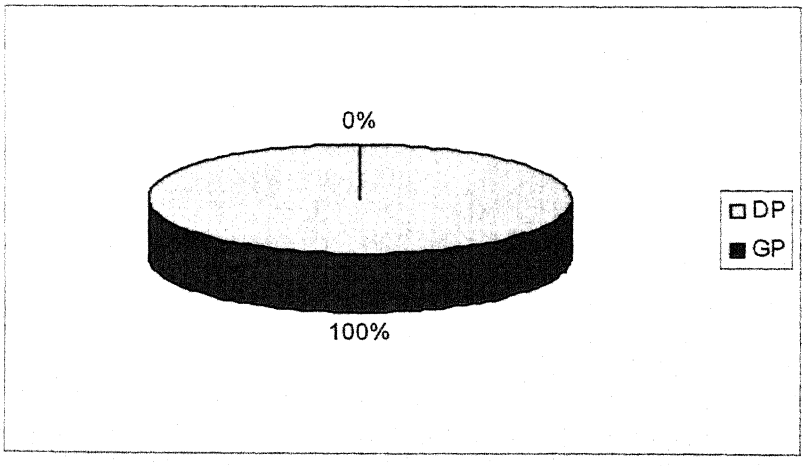
PATIENTS WITH DUODENAL PERFORATION & GASTRIC PERFORATION

TABLE NO. 14

NUMBER OF CASES OF DP AND GP	DP	GU
	25	0

In this study all the patients of perforation found to have duodenal perforation, and no case of gastric perforation was found.

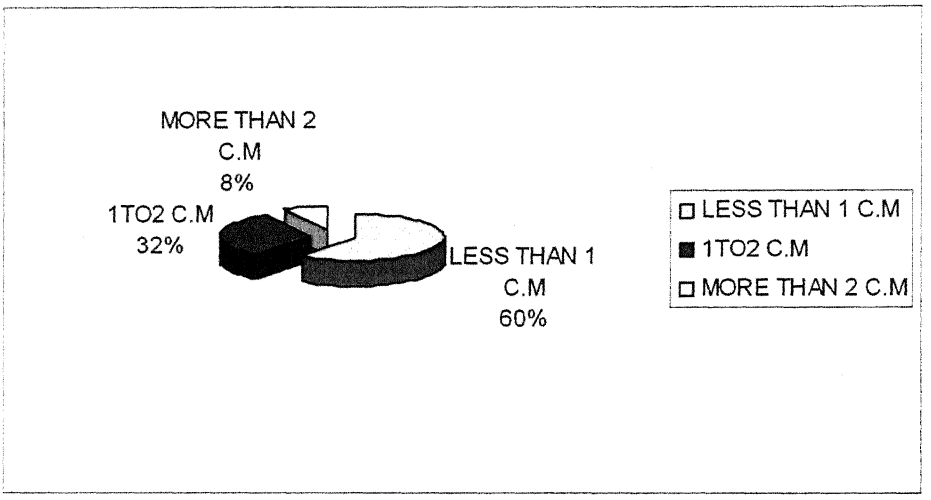




PATIENTS WITH DIFFERENT SIZE OF PERFORATION

TABLE NO. 15

SIZE OF PERFORATION	LESS THAN 1 C.M	1 TO 2 C.M	MORE THAN 2 C.M
	15	8	2

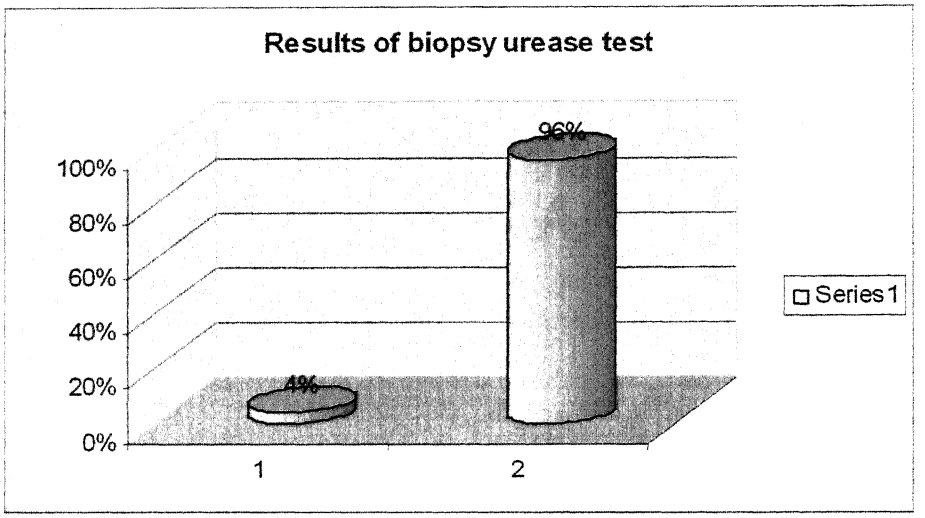


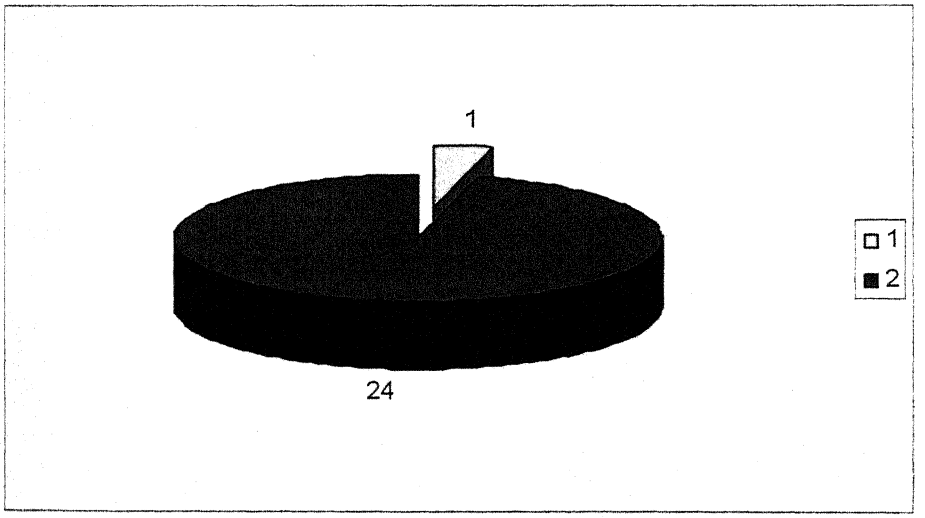
RESULTS OF BIOPSY UREASE TEST IN STUDY

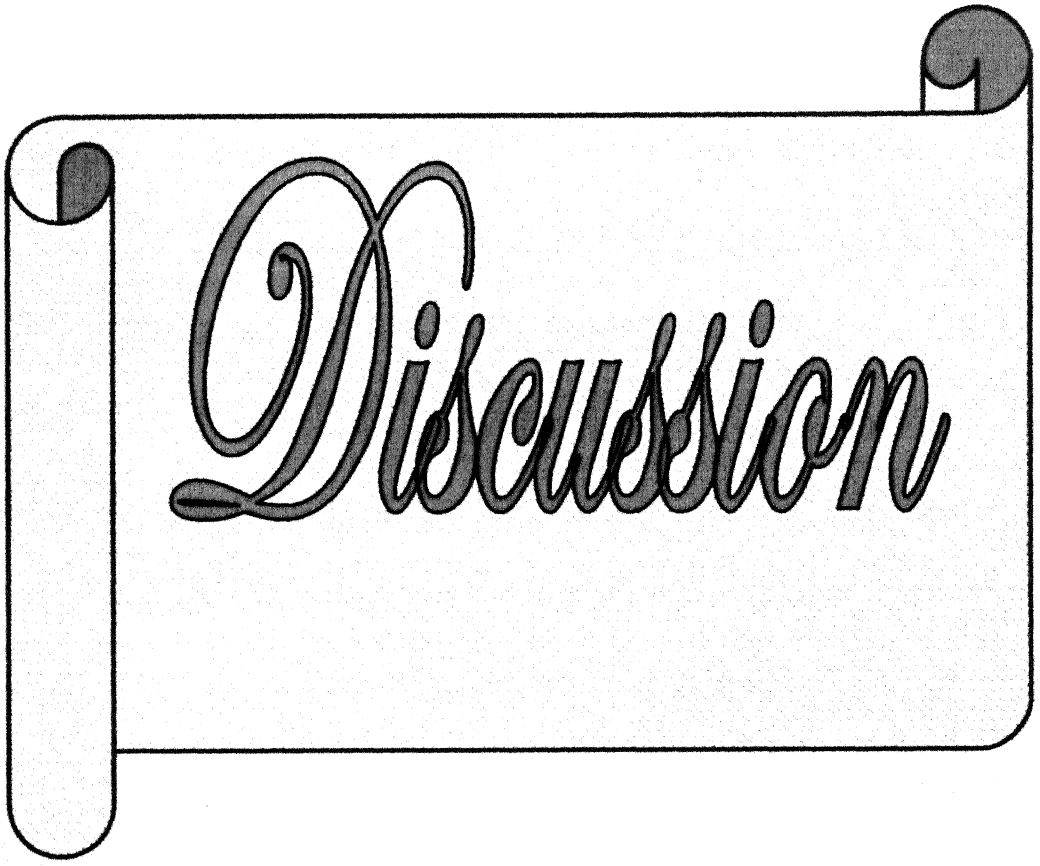
TABLE NO. 16

Results	No. of patients
Positive	24
Negative	01

So, 24 patients out of 25 patients shown positive result (96%).






Discussion

DISCUSSION

AGE DISTRIBUTION

In the present study of 25 cases the highest incidence of perforated peptic ulcer was between 30 to 60years, 72 (%) of patient fell in this group. A study done on 23 patients at EAST BIRMINGHAM HOSPITAL in 1981-82 showed the mean age of presentation of 56 years. This might be due to the different trends of this entity in the Western countries where the elderly patients are the primary victims. Various case series in India and abroad have mean age of presentation between 40-60 years, and in our study between 30-60 years.

College, Shimla in 1983-92, showed the mean age of presentations between 41-50 years, this is consistent with that of our study.

A study on perforated peptic ulcer done in JLN Medical College Ajmer RAJISTHAN, showed the maximum age incidence between 30-40 years, this figure is again compatible to our study.

GENDER DISTRIBUTION

In the present study the entire patient were male and non of the patient was female. Because of the small sample size and short duration over which the study has been done precludes any possible explanation for this.

A study in IG Medical College Shimla over the period of 10 years from 1983-1992, showed male to female ratio of 17,1. This ratio shows the very high incidence in male patients, which is shown in our study.

A prospective study done in JLN Medical College, AJMER (RAJASTHAN), on 43 patients, all the patients in that study were male and none of patient were female. Various other study conducted abroad confirms the increasing

incidence as well as a very high incidence of perforated peptic ulcer in male gender.

H/O SMOKING

In our study 64(%) patients were smoker majority of them were smoking 20 biree /day and 36(%) were non-smoker. Although erratic, it seems that disease incidence is increasing among non-smokers. The association of smoking to peptic disease does not need emphasizing. These data's shows the finding of multi factorial etiology of peptic ulcer disease. , Although our study shows a strong association of smoking and peptic perforation.

H/O ALCOHOL INTAKE

In our study out of 25 patients only 5 patients were alcoholic (20%), and 20 patients were non- alcoholic (80%). Out of 5 patients 3 patients were occasional drinkers.

No study available shows association between alcohol intake and peptic ulcer perforation.

In our study there is no more increased incidence of peptic ulcer perforation in smoker group than non-smoker group, so we could not ascribe a cause for this in our study.

ECONOMIC STATUS

In our study 19 patients (76%) were from poor socioeconomic status, and 6 patients were from average economic status.

So, in our study 76% patients were from poor socioeconomic status. So, in our study it seems that peptic ulcer perforation are more common among poor socioeconomic group patients.

This fact is validated from other studies, which have shown similar association between poor economic status and peptic ulcer perforation.

FOOD HABITS

In our study 60% patients were vegetarians and 40% patients were non vegetarians, so on conclusive evidence can be drawn from these data's.

LIFE STYLE

In our study 60% patients were from moderate worker and 40% patients were from hard worker group.

So from these data's no conclusive evidence can be drawn from this study.

EDUCATION STATUS

In our study only 2 patients were educated above 10th class rest 23 patients (92%) were poorly educated and most of them are non-educated.

So from these data's it seems that perforated peptic ulcer is more common in poorly educated and patients from poor socioeconomic status.

OCCUPATION

In this study 23 (92%) patients were farmer. So, from above data's can be safely said that in Bundelkhand region the perforation is more common in farmers with poor economic status and poor education status.

ASSOCIATION WITH OTHER MEDICAL PROBLEMS

In our study only 1(4%) patient was suffering from Tuberculosis of lung and rest were non-tubercular.

Only 3(12%) patients were hypertensive and rest 22(88%) patients were normotensive.

No patient was suffering from Ischimic heart disease and Diabetes mellitus.

So from above mentioned data's it seems that these diseases have nothing to do with perforated peptic ulcer, they are no more common in perforated peptic ulcer then from general population.

SIZE OF PERFORATION

In our study size of perforation was less than 1 cm in 15(60%) patients and 1-2 cm in 8(32%) patients, only 2(8%) patients were having perforation size more than 2 cm.

RADIOLOGICAL FEATURES

In this study all the cases were having gas under diaphragm in there, x-ray abdomen erect view.

In one study conducted in J.L.N. Medical College Ajmer 8.25 patients plain skiagram abdomem in erect view did not demonstrated free gas under diaphragm.

The demonstration of pneumoperitonium following perforated viscus is however not invariable and most series show that in only 75-80 of perforation is free gas demonstration. A number of reason for this have been suggested including:-

1-Sealing of perforation.

2-Lack of gas, at the site of perforation.

3-Adhesion around perforation.

4- Faulty technique.

However radiographic technique and positioning is also important and it is recommended that a patient should

be in position for 10 mins, prior to film taken for it takes this time for free gas to rise to highest point in the abdomen, however it is not possible in abdominal catastrophe and it is seldom practiced by the radiologist.

If left lateral decubitus projection is included, this yield can be increased up to 90%, which is similar to sensitivity of U.S.G to demonstrate pneumoperitonium.

Relation between H. pylori and perforated ulcer.

RESULTS OF BIOPSY UREASE TEST

In our study out of 25 patients 24 (96%) patients were positive for biopsy urease test.

Metzger et al study reported a prevalence of 73% of H pylori infection in perforated peptic ulcer.

Papaziogas B, Pavlidis T, et al reported a prevalence of 62.5%of H pylori in perforated peptic ulcer.

Annals of surgery 231(2); 153-158, feb 2000,

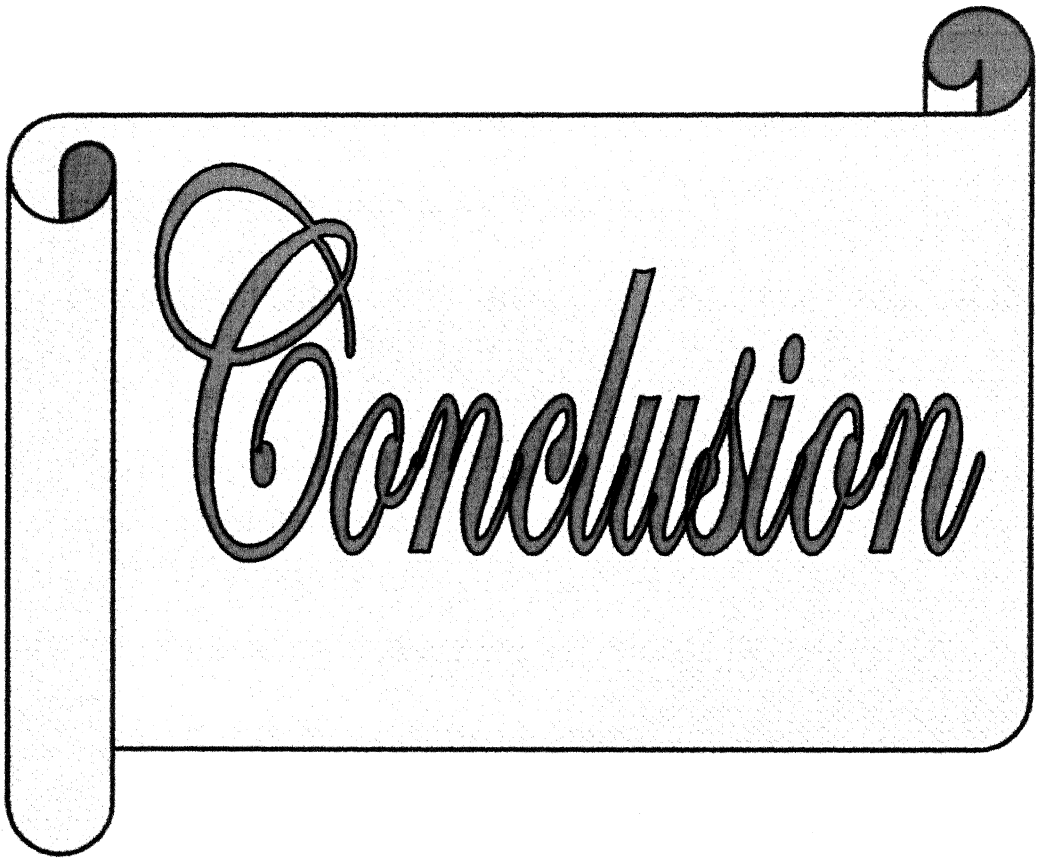
Ng, Enders K.W.MD, LAM, Y.H.MD et al reported a prevalence of 81% in perforated peptic ulcer.

Department of gastroenterology, PG institute of medical education and research, Chandigarh, India. Conducted study on 45 pts, 15 (34%) pts were in group of perforated peptic ulcer, none of them tested positive for H. pylori infection.

In our study results are very different from the other mentioned studies, quoted above.

So in our study perforated peptic ulcer are clearly associated with H. pylori infection as a strong etiological factor.

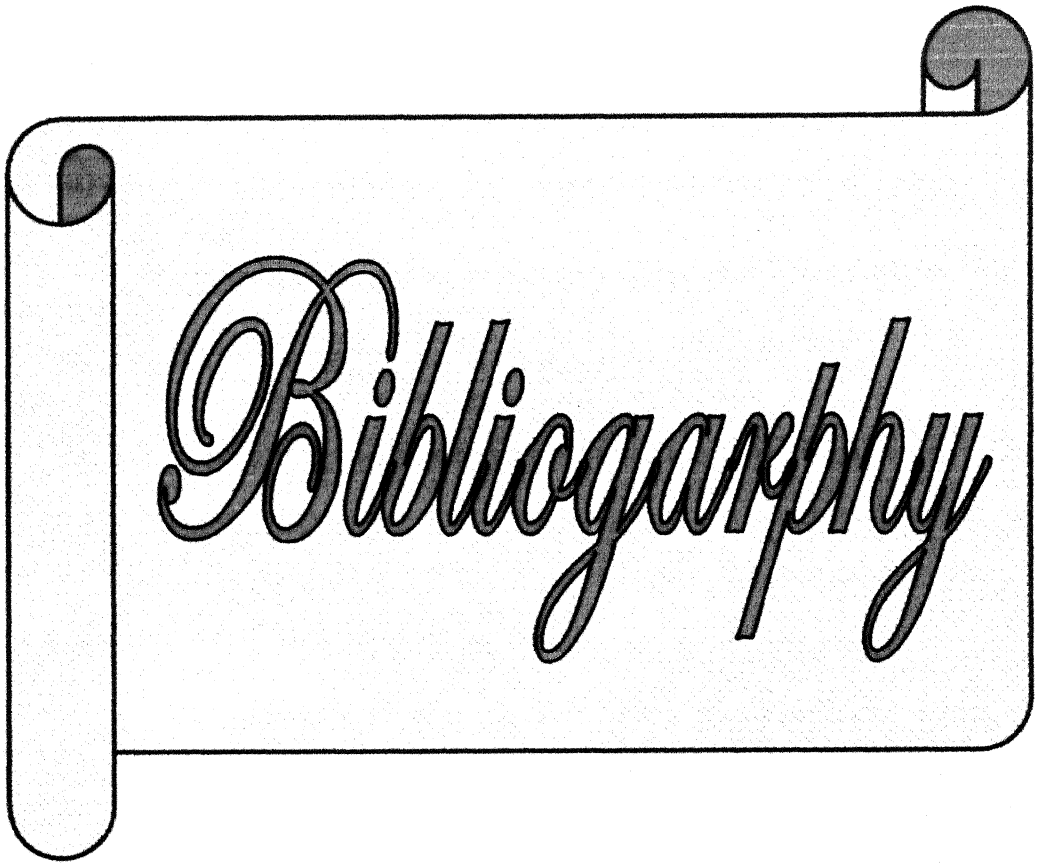
No patients returned back for follow up endoscopy and biopsy.


Conclusion

CONCLUSIONS

1. Most common peptic perforation was duodenal perforation.
2. Commonest age of presentation of peptic perforation in Bundelkhand region was 30-60 years.
3. Most commonly mans were affected with the ratio of 25;0.
4. Most of patients (76%) were from poor socioeconomic status.
5. Most of patients (64%) were chronic smoker.
6. Most of patients were non- alcoholic (80%).
7. Almost half of the patients were vegetarians.
8. Almost half the patients were hard worker and half were moderate worker.
9. Almost all the patients (92%) were poorly educated.
10. Almost all the patients (92%) were farmer by occupation.
11. Almost all the patients (88%) were normotensive.

12. All the patients were non-diabetic.
13. Non of the patient was suffering from Ischimic heart disease.
14. Almost all the patients (96%) were non Tubercular.
15. Family history could not be elicited in any of patient.
16. No patient gave history of chronic NSAIDS use.
17. Gass under diaphragm was a significant finding in erect X-ray of abdomen in perforated peptic ulcer.
18. Almost all the patients (96%) were infected with H. pylori detected by Biopsy urease test.
19. It can be concluded that H. pylori may be the causative factor for perforation of peptic ulcer.
20. In all factors studied H. pylori was most closely associated factor with perforated peptic ulcer.
21. So eradication of H. pylori may reduce the reoccurrence of peptic perforation.


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